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Geographical variation in neonatal size and shape, and relationships with maternal and paternal body composition

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ABSTRACT

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GEOGRAPHICAL VARIATION IN NEONATAL SIZE AND SHAPE, AND RELATIONSHIPS WITH MATERNAL AND PATERNAL BODY COMPOSITION

By Samantha Dawn Leary

Studies demonstrating a relationship between small size at birth and adult cardiovascular disease suggest an improvement in fetal growth may lead to reductions in adult disease. The size and body proportions of the baby at birth are partly determined by maternal body composition. Most studies have only considered maternal height and weight, and their relationships with neonatal birthweight, so a clearer understanding of this area is required. Paternal size and body composition also play a role, primarily through the fetal genome, although few studies have investigated father to baby relationships. This thesis uses a number of datasets to characterise geographical variation in neonatal and maternal phenotypes, and investigate both maternal-neonatal and paternal-neonatal relationships. These include cohorts from UK, Finland, India, Sri Lanka, China, Congo, Nigeria and Jamaica. Analyses were restricted to singleton, liveborn, term births.

Neonates in Europe were the largest, followed by Jamaica, China then Africa, India and Sri Lanka. There was wide variation in many of the measurements such as birthweight, where the mean values ranged from 2730g to 3570g across populations. However, head circumference was similar in all populations except China, where it was markedly smaller. The main differences between populations were in the ratio of head to length, with small heads in China and large heads in India, Sri Lanka and Africa, relative to length. The mothers from Sri Lanka were the shortest (mean height 151cm) and thinnest (mean BMI at 30 weeks gestation 20 kg/m^2), while those from Southampton were the tallest (mean height 164cm) and fattest (mean BMI 27 kg/m^2). There were large differences between mothers in the amount of fat relative to muscle. Urban Indian mothers were relatively fat while mothers from the Congo, rural India and particularly Jamaica were relatively muscular.

Mother to baby relationships were surprisingly similar across populations, although some effects were stronger in developing countries. All the maternal variables had important effects on the neonatal measures, particularly maternal birthweight. 'Like with like' relationships were seen consistently for maternal height and neonatal length, maternal and neonatal head, and maternal and neonatal fat. Maternal muscle effects were relatively weak, except in one dataset (Congo). After adjusting for the variation in maternal phenotypes across populations, differences in neonatal phenotypes were reduced but still present. Paternal height had the strongest effect on neonatal length, while effects of paternal BMI were generally similar across the neonatal measures. When compared with maternal height and BMI, paternal effects were weaker in most datasets.

As maternal body composition was shown to explain a large part of the geographical variation between neonates, and all the maternal variables had independent effects on neonatal phenotype, this implies that nutrition during the whole of the mother's life cycle influences fetal growth, not just her body composition during pregnancy. As paternal size also influenced neonatal phenotype, although to a lesser extent, this is likely to reflect genetic effects, which appear to be stronger for the skeleton than the soft tissues.

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Author's contribution

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Abbreviations

AMA	Arm muscle area
ANOVA	Analysis of variance
BMI	Body mass index
CHD	Coronary heart disease
CH length	Crown-heel length
CR length	Crown-rump length
CSD	Caesarean section delivery
CV	Coefficient of variation
HMH	Holdsworth Memorial Hospital, Mysore, India
IGT	Impaired glucose tolerance
IQR	Inter-quartile range
IUGR	Intrauterine growth retardation
KEM	King Edward Memorial Hospital, Pune, India
LMP	Last menstrual period
MRC EEU	Medical Research Council Environmental Epidemiology Unit
MUAC	Mid-upper-arm circumference
NIDDM	Non-insulin dependent diabetes
NVD	Normal vaginal delivery
PCA	Principal components analysis
PC	Principal component
PI	Ponderal index
SBP	Systolic blood pressure
SD	Standard deviation
UK	United Kingdom
WHO	World Health Organisation

Dataset names used in graphs:

Soton	Southampton
IOM	Isle of Man
King	Kingston

1 Introduction

Coronary heart disease (CHD) is the leading cause of death in developed countries, and incidence is rising in developing countries. Small size at birth has been shown to be associated with CHD, so it is important to understand the determinants of fetal growth. Maternal size and body composition are known to influence fetal growth, so detailed knowledge of mother to baby relationships is required. Paternal size and body composition also play a role, through the fetal genome, so father to baby relationships are of interest.

1.1 Size at birth and disease in adult life

1.1.1 Incidence of coronary heart disease and associated disorders

In 1990 there were more than 50 million deaths worldwide, and CHD was the leading cause at more than 6 million. Almost 40 million of the deaths occurred in developing countries, and of these, just under 4 million were due to CHD (Murray and Lopez 1997). Rates of mortality from CHD are predicted soon to overtake those from infectious diseases in developing countries such as India (Bulatao and Stephens 1992).

Non-insulin dependent diabetes (NIDDM) is one of the disorders associated with CHD. In 1995, the worldwide prevalence was estimated to be 4% (135 million), and was higher in developed than developing countries (King 1998). This prevalence is rising steeply particularly in developing countries, with rapid urbanisation. Other disorders associated with CHD include hypertension, adverse profiles for lipids such as cholesterol and triglycerides, and also high fibrinogen levels.

1.1.2 Established risk factors

The rapid increases in CHD incidence over a short time cannot be explained by genetic mechanisms, and research has concentrated on the effect of adult lifestyle factors. Established risk factors for CHD include cigarette smoking, high intake of dietary fat, physical inactivity, obesity and stress. However, using these to explain the disease leads to a number of inconsistencies.

In the UK, the increase in CHD has been associated with increasing affluence, and yet the disease is now more common in poorer areas and lower income groups. In many Western countries, the steep rise in incidence has been followed by a fall, and although there have been changes in adult lifestyle, these were predated by the fall. For men in the United Kingdom (UK) in the lowest group for risk factors such as cholesterol concentrations and blood pressure, the commonest single cause of death is still CHD (Rose 1985). India is experiencing an epidemic of CHD even though cigarette smoking, especially among women, and high dietary intakes of saturated fat are uncommon. These are all indications that other risk factors may be involved.

1.1.3 Fetal origins hypotheses

Forsdahl (1977) first described a direct geographical association between CHD mortality in the years 1964-67 and infant mortality 70 years earlier in Norway. He attributed this to poor childhood environments causing some form of permanent damage, and suggested it would lead to a lifelong vulnerability to certain affluent adult lifestyle factors such as high dietary fat intakes.

Barker and colleagues then suggested that CHD might be linked to impaired fetal growth, rather than childhood growth as previously suggested by Forsdahl. It was observed that CHD mortality in parts of England and Wales paralleled infant mortality in the early part of last century (Barker and Osmond 1986). Neonatal mortality is a reflection of fetal experience in the intra-uterine environment, and is inversely related to size at birth. The 'fetal origins hypothesis' states that adaptations made by the fetus in response to undernutrition permanently change or 'programme' its physiology, metabolism and structure (Barker 1998a). This may predispose individuals to a number of diseases in adult life, including CHD and its associated disorders. The effects of these programmed changes may be magnified by factors in postnatal life, such as obesity.

1.1.4 Summary of evidence

Weight at birth and in infancy

The first direct evidence that CHD may originate in-utero came from a follow-up study based on birth records from Hertfordshire, England. It was demonstrated that low birthweight, and also low weight in infancy (men only) were associated with higher rates

of cardiovascular disease in adult life (Barker et al. 1989, Osmond et al. 1993). Inverse relationships between birthweight and cardiovascular disease have also been found in men in Sheffield, England (Barker et al. 1993a, Martyn et al. 1996), Caerphilly, Wales (Frankel et al. 1996) and Helsinki, Finland (Forsén et al. 1997), women in the USA (Rich-Edwards et al. 1997), and both sexes in Uppsala, Sweden (Leon et al. 1998) and Mysore, India (Stein et al. 1996). Relationships were seen across the whole range of birthweights, and were independent of the length of gestation, implying that small size at birth was reflecting lower rates of fetal growth as opposed to prematurity (Leon et al. 1998). In addition, they could not be explained by adult lifestyle factors.

Low birthweight has consistently been associated with other risk factors for CHD such as an adverse profile of glucose and insulin metabolism (Newsome et al. in press), and raised blood pressure (Huxley et al. 2000) in later life. Inverse relationships have also been shown with levels of triglycerides in men (Frankel et al. 1996, Lithell et al. 1996) and children (Donker et al. 1997). Relationships with adult fibrinogen levels are less consistent; both inverse associations (Martyn et al. 1995) and direct associations (Frankel et al. 1996) have been shown for men.

Other body measurements at birth

The majority of studies consider only birthweight when investigating the relationship between size at birth and disease in later life. However, adult cardiovascular disease was associated with short length and small head size at birth in men in Sheffield (Barker et al. 1993a, Martyn et al. 1996) and men and women in Mysore (Stein et al. 1996). It was also associated with low ponderal index (PI) which is a measure of thinness defined as weight relative to height in men in Sheffield (Martyn et al. 1996) and Helsinki (Forsén et al. 1997).

There is also some evidence that shortness or thinness at birth is associated with adverse levels of glucose and insulin. Flanagan et al. (2000) showed that men who were short at birth were more insulin resistant as adults, although this relationship was not seen in women. Thinness at birth was associated with raised insulin resistance, impaired glucose tolerance (IGT) and NIDDM (Phillips et al. 1994) in Preston, and with raised insulin levels and NIDDM in men in Uppsala (Lithell et al. 1996). Relationships were also seen with raised glucose levels in adults in Amsterdam (Ravelli et al. 1998) and children in Salisbury (Law et al. 1995).

Huxley et al. (2000) have reviewed studies investigating relationships between body proportions at birth and blood pressure in later life. These were less consistent that those seen with birthweight, although some showed inverse relationships with head size, length and PI. Only three studies measured chest circumference, and the findings were inconsistent. Since this review, Law et al. (2000) have measured blood pressure in children aged 3-6 in five countries. They found that those who were proportionately small in China, Chile and Guatemala had raised blood pressures, while thinness at birth was associated with higher blood pressures in Sweden. There was no relationship between size at birth and later blood pressure in Nigeria.

In Sheffield, abdominal circumference, and to a lesser extent other dimensions at birth were inversely related to adult levels of fibrinogen in men but not women (Martyn et al. 1995) and low-density lipoprotein cholesterol in both sexes (Barker et al. 1993b). This was the only study which included measurement of abdominal circumference.

Placental weight

Godfrey (2002) has reviewed the literature on relationships between placental weight and also placenta to birthweight ratios, and disease in later life. Low placental weight was associated with adult CHD in men in Helsinki (Forsén et al. 1997), although other studies did not find any relationships. A high placenta to birthweight ratio was found to be associated with later CHD in women in Helsinki (Forsén et al. 1999), while a U-shaped relationship was seen in men in Sheffield, such that both low and high placenta to birthweight ratios were associated with CHD in adult life (Martyn et al. 1996). Forsén et al. (2000) found an increase in the prevalence of NIDDM in Helsinki amongst those who had light placentas, and Phipps et al. (1993) showed that high placenta to birthweight ratios were associated with IGT in Preston.

Relationships between placental weight and later blood pressure were seen in a number of studies, although the direction of the relationship was inconsistent. Inverse relationships were seen in Aberdeen (Campbell et al. 1996), and Helsinki (Eriksson et al. 2000), although only in those with diabetes, while in Preston the relationships were direct (Barker et al. 1990). Heavier placentas were also associated with raised blood pressure in childhood in Salisbury, Adelaide and a survey of 10 towns in England and Wales (Law et al. 1991, Moore et al. 1996, Taylor et al. 1997). High placenta to birthweight ratios were associated with raised blood pressure in adults in Preston, Adelaide and Helsinki (Barker

et al. 1992a, Moore et al. 1999, Eriksson et al. 2000), although only in non-diabetics in the latter. No relationships with these ratios were seen in children in Guildford and Carlisle (Whincup et al. 1995).

An inverse relationship was shown between placental weight and fibrinogen levels in Sheffield men but not women (Martyn et al. 1995), while the placenta to birthweight ratio was directly related to fibrinogen levels in men in Hertfordshire (Barker et al. 1992b).

Conclusion

The patterns of growth that may lead to CHD, and associated disorders in later life are complex, and may differ by sex and within and between ethnic groups. Studies of relationships between low birthweight and adult disease have been extensively replicated in different populations, and are not the result of confounding variables. However, relationships with other body proportions at birth are less consistent, so possible reasons for these differences across populations are of interest.

1.2 Characterisation of phenotypes

1.2.1 Neonatal phenotypes

Birthweight

Size at birth is a function of the rate of growth of the fetus and the duration of gestation. Birthweight is a crude summary measure of size, which includes length, head, muscle, adipose tissues and internal organs. For example, use of birthweight alone may not distinguish between a short fat and a long thin neonate. However, despite the pitfalls of using birthweight as a summary of fetal growth, it has the major advantage that measurements can be made with reasonable accuracy in the widely varying conditions of obstetric practice throughout the world.

Traditionally, low birthweight has been defined as a birthweight less than 2500g. The prevalence of low birthweight is 19% in developing countries compared to 7% in developed countries (WHO 1992). The highest prevalence rates are in South Asia, for example in India, 28% of neonates are born with low birthweight, although values vary widely even between developing countries. The mean birthweight in India is 2600g, compared to 3200g in the UK (WHO 1995). However, these figures include pre-terms

born before 37 weeks, as well as those who were growth retarded. Prevalence rates for pre-term births are 10% and 5% for India and the UK respectively (WHO 1995). The World Health Organisation (WHO) now recommends that intrauterine growth retardation (IUGR), defined as a birthweight below the 10th percentile of the birthweight-for-gestational-age reference curve should be used in preference to low birthweight (de Onis et al. 1998). Prevalence rates of IUGR are higher than those for low birthweight, for example in India the rate is 54% (de Onis et al. 1998).

Other body measurements at birth

Anthropometric measurements can be used to assess some of the individual components of birthweight. The size of the skeleton can be quantified by length measurements such as crown-heel (CH), crown-rump (CR) and leg. Head circumference is another 'skeletal' measurement, but it has been suggested that it can also be used as a proxy for brain size. Head to length or head to abdominal ratios have been used to identify 'brain sparing', where brain growth is spared at the expense of other tissues, as a response to fetal undernutrition. Abdominal circumference has been suggested as a proxy for liver size (Barker 1998b), and chest circumference may also be measured, although is less useful as fat, skeleton and lung growth are all included in the measurement. Mid-upper arm circumference (MUAC) can be used to assess the degree of muscularity, although fat and bone is also included in its measurement. Arm muscle area (AMA) and muscle mass can be calculated (Jelliffe and Jelliffe 1960) to overcome this difficulty to some extent. Skinfold measurements are direct measures of fat, with triceps and biceps measuring peripheral fat, and subscapular and suprailiac measuring central fat. The percentage of fat, and also fat mass can be calculated using these measurements (Durnin and Womersley 1974). Ponderal index (Livi 1897), calculated from birthweight and length can also be used as an indicator of fatness, although this does not distinguish between variations in fat and muscle, or quantify visceral weight.

The mean CH length and head circumference for a neonate born at 40 weeks gestation in India are 49cm and 34cm respectively (Mohan et al. 1990). These values are 52cm for CH length and 35cm for head circumference in the UK (Gairdner and Pearson 1971). However, detailed comparisons of body proportions at birth in different populations do not exist.

Placental weight

The weight of the placenta may give an indirect measure of its capacity to transfer nutrients and oxygen to the fetus (Sanin et al. 2001). The ratio of placental weight to birthweight has been suggested as a marker of placental efficiency, with low ratios indicating a more efficient placenta.

1.2.2 Maternal phenotypes

Anthropometric measurements

A mother's nourishment during her own fetal life is reflected in her birthweight, while her experiences in infancy are reflected in her adult head size (Shea 2000), and in childhood reflected in her adult height. Pre-pregnancy muscle mass obtained from measurements of MUAC and triceps skinfold provides an indication of the mother's current protein reserves. Pre-pregnancy fat mass obtained from skinfold measurements indicates the mother's current energy reserves. Hence a mothers' weight is a composite of her nutritional experiences throughout her whole life. Body mass index (BMI) (Quetelet 1869) can be calculated to represent weight independent of stature.

Little information is available on geographical variation in maternal size and body composition other than height and weight. The mean heights and weights for females in India are 151.7cm and 42.4kg respectively (ICMR 1984), compared with 161.0cm and 68.8kg in England (Department of Health 2000).

Changes during pregnancy

Weight gain during pregnancy includes both fat-free and fat components. The fat-free component includes breast and uterine tissue, increased blood volume, and also the fetus, placenta and amniotic fluid. The fat component has been shown to increase most in central areas (suprailiac, subscapular) peaking at 30 weeks gestation, and least in the periphery (biceps, triceps) (Taggart et al. 1967). The mother lays down fat stores in the first half of pregnancy, and this is a major source of energy to her fetus in late gestation. The skeleton has been shown to change little during pregnancy (Brozek 1973).

In developed countries, approximate weight gain is 1.5kg at 10 weeks, 4kg at 20 weeks, 8.5kg at 30 weeks, and 12.5kg in total (Hytten and Leitch 1971). Few studies of body compositional changes during pregnancy have been conducted in developing countries

where women are less nourished, although those that exist show that changes are much smaller. Winkvist et al. (2002) found that total mean weight gain was 8.3kg in their Indonesian study, and that 79% of the women did not meet the recommendation regarding ideal weight gain for their BMI before pregnancy.

1.3 Fetal growth

1.3.1 Stages of growth

The embryo comprises two groups of cells; the outer cell mass that becomes the placenta, and the inner cell mass that becomes the fetus. During early gestation (up to 18 weeks), cells divide and enlarge, then differentiate into structures that form specific tissues that come together to make organs. Throughout mid gestation (18 to 28 weeks), cell division continues at a slower rate, with an increase in cell size that continues throughout late gestation (28 weeks until term), although during this time cell division slows further.

Different fetal tissues and organs have different periods of rapid growth where rapid cell division occurs, and these are known as 'critical periods'. The skeleton grows in early gestation, and the head is established first. Although peak velocity has already occurred, length continues to increase throughout mid gestation. The soft tissues, including muscle and fat develop in later gestation. Placental growth is most rapid at the beginning of gestation, and continues until near term. The weight of the fetus increases throughout gestation, although peak velocity is reached in late gestation. The contrast between peak velocity for length and weight growth is illustrated for boys in Figures 1.1a and b (Tanner 1989).

Figure 1.1a Velocity curve for CH length

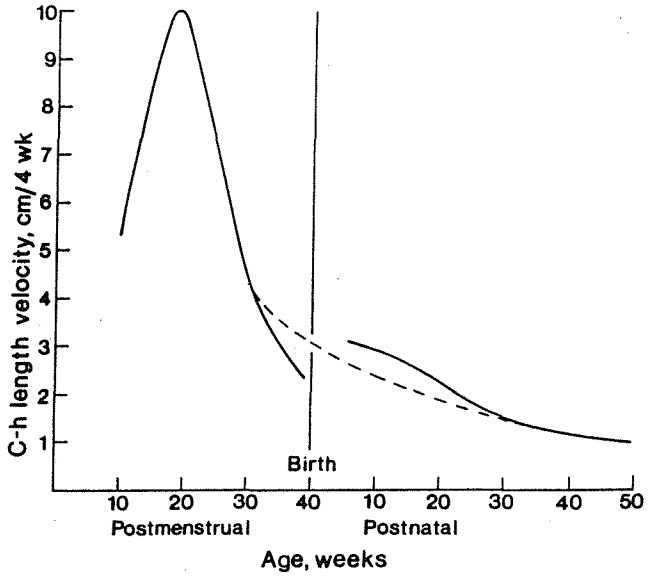
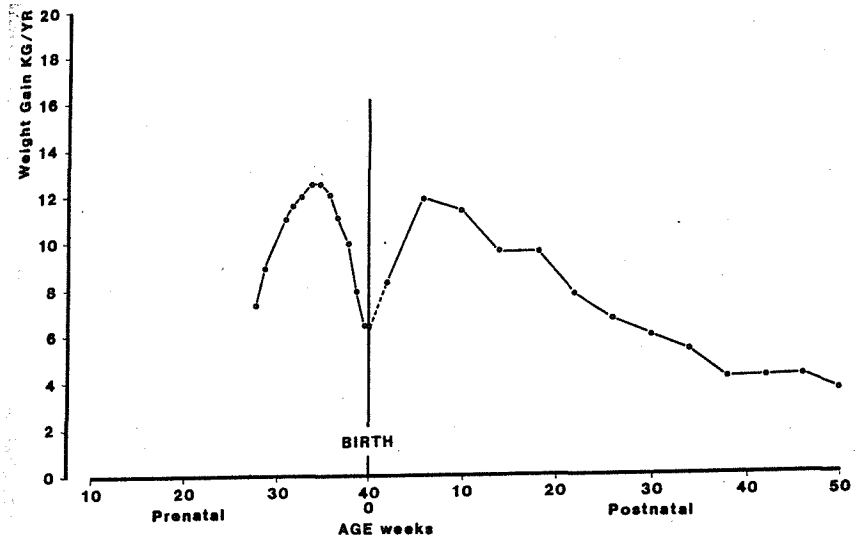


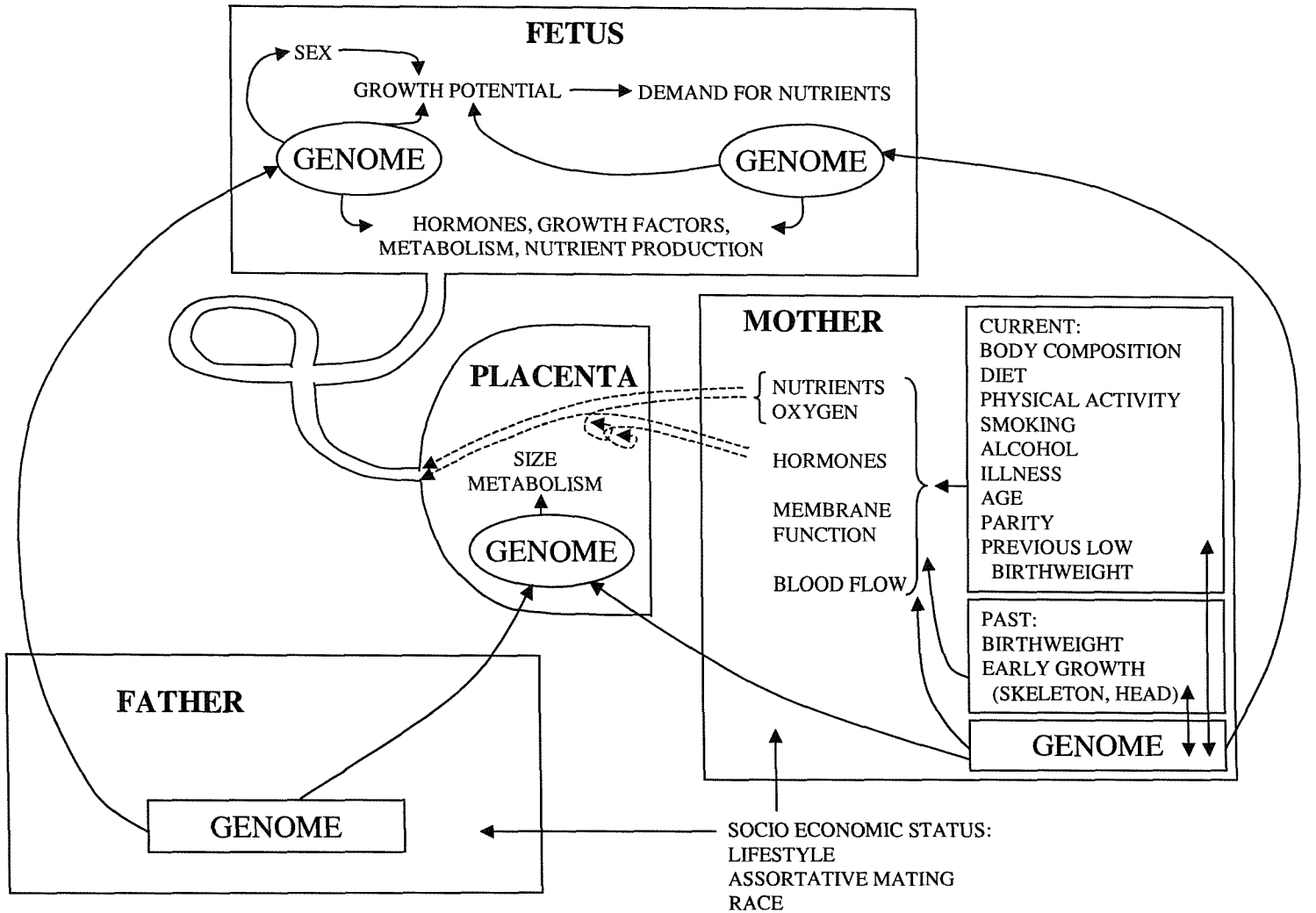
Figure 1.1b Velocity curve for fetal weight

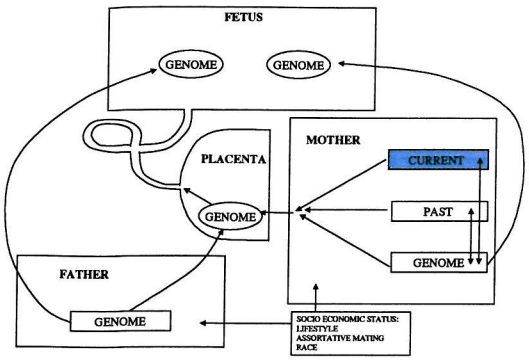


1.3.2 Mechanisms of growth

Size at birth reflects the growth trajectory of the fetus, which is directed by genes inherited from both parents, but limited by its intra-uterine environment. The supply of nutrients and oxygen to the fetus depends on a number of maternal factors to varying extents, such as body composition and diet, as well as the adequacy of transportation across the placenta. Figure 1.2 illustrates the complex interactions between factors that determine size at birth.

Figure 1.2 Factors influencing fetal growth





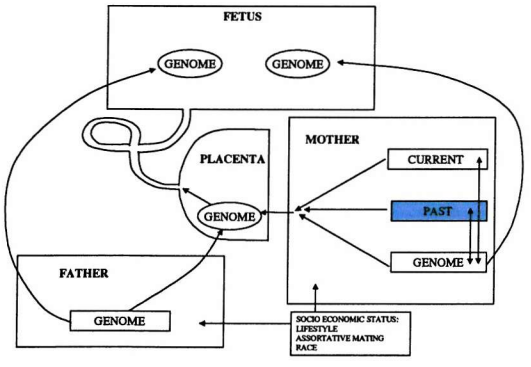
Maternal height and weight have been shown to have an effect on neonatal birthweight in a large number of studies, with the shortest, thinnest mothers who gain least weight through pregnancy having the smallest babies (Kramer 1987). A few studies have also examined the effect of maternal body measurements other than height and weight, such as muscle and fat (Neggers et al. 1995) and also head circumference (Bhatia and Tyagi 1984), which were all shown to be directly associated with neonatal birthweight. Most have only investigated effects on weight rather than other body proportions at birth, although some studies have shown direct relationships between measures of maternal muscle and fat, and neonatal length, head size, and degree of muscularity or adiposity. These were based in both developed countries (Whitelaw 1976, Neggers et al. 1995, Silliman and Kretchmer 1995) and developing countries (Frisancho et al. 1977, Sibert et al. 1978, Swain et al. 1991, Ricalde et al. 1998). There were differences in the strengths of relationships across these studies, which may have been due to geographical differences in maternal body composition.

Maternal diet is likely to vary widely across populations. Few studies have assessed the effect of poor maternal diet during pregnancy on birthweight, and results have not been consistent. In adequately nourished populations, effects of maternal supplementation trials of both micronutrients and macronutrients on neonatal birthweight have been weak or non-significant (Kramer 1993). However, if maternal food intake during pregnancy is severely restricted, for example during the Dutch 'hunger winter' of 19944/45, effects on birthweight in the order of 300g have been shown (Stein et al. 1975). Limited information is available regarding effects on measurements at birth other than weight, although reduced dairy protein in pregnancy has been shown to be associated with shortness or thinness at birth (Burke et al. 1948, Godfrey et al. 1997). Also, Dutch babies exposed to wartime famine in mid or late gestation were shorter with smaller head circumferences (Stein et al. 1975). The study of energy supplementation of mothers in the Gambia, which showed increases in neonatal birthweight during the wet season when food is scarce and workload increases, is currently the only good quality evidence from a developing country (Prentice et al. 1987).

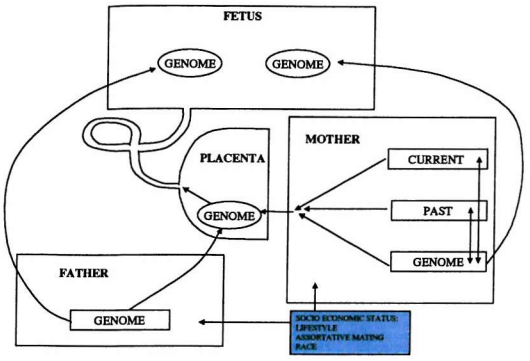
Physical activity levels vary according to the population, and these have been inversely related to neonatal birthweight in some studies, mainly in developing countries where mothers may be required to undertake strenuous work and are undernourished (Kramer 1987). Lifestyle factors have also been shown to play a role; mothers who consumed large amounts of alcohol had lighter babies, as did those who smoked (developed countries), or chewed tobacco (developing countries) (Kramer 1987).

In developing countries, general morbidity through episodic illness may lead to lower birthweights (Kramer 1987). Another particular problem for developing countries is the high incidence of infectious diseases such as malaria, which increase the risk of lower birthweight. On the other hand, maternal diabetes may increase the risk of macrosomia. With the exception of women who develop severe pre-eclampsia or severe hypertension, only one study has found an association between maternal blood pressure and birthweight, whereby high blood pressures were associated with lighter babies (Churchill et al. 1997). Weaker effects on both PI and head size at birth were also shown.

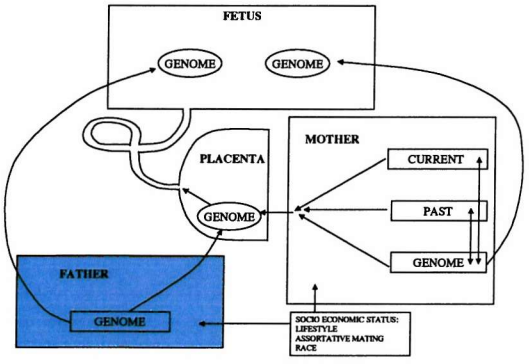
Older mothers have been shown to have heavier babies, as do those of higher parities, although as these are obviously correlated with each other, effects may not be independent (Kramer 1987). Having previous low birthweight babies has also been associated with an increased risk of giving birth to a lower birthweight baby, although this relationship has only been investigated in developed countries (Kramer 1987).



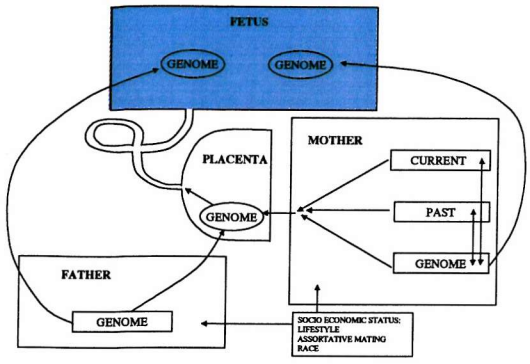
It is not only current factors relating to the mother that affect size of the baby at birth. The mother's own birthweight has been shown to be directly related to that of her offspring, and Ramakrishnan et al. (1999) describe a number of studies that demonstrate this, although almost all are from developed countries. Godfrey et al. (1997) have also have found that mothers from Southampton who themselves were light at birth had babies who were thin, while Ramakrishnan et al. (1999) reported a direct relationship between maternal birthweight and neonatal length in their Guatemalan study.



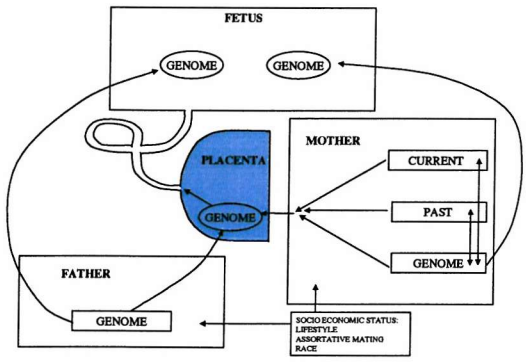
The father may influence some factors that affect fetal growth through the mother. Socio-economic status, which is primarily determined by education, occupation and income of both parents, and again is widely variable across populations, has been shown to affect birthweight, with mothers in lower social classes having lighter babies (Kramer 1987). Lifestyle factors may also be influenced by the father, for example a woman is more likely to smoke if her husband does, or at least be a passive smoker. Assortative mating, when 'like tend to marry like' is common in developing countries such as India where similarity of height may be a criterion for arranged marriages. However, it is also common in Western countries (Mascie-Taylor 1987), possibly as a result of personal choice, but may also be explained by similarity in background variables such as social class, which has been shown to be associated with height (Mascie-Taylor and Boldsen 1985). Relationships between ethnic group and birthweight have been demonstrated in a number of studies (Kramer 1987), with the lowest birthweight babies being born to Indian or Black mothers, although this may be due to other confounding factors such as social conditions.



A small number of studies, mostly based in developed countries have shown that paternal size is associated with weight of the baby at birth, with shorter, lighter fathers having lighter babies, although effects were weaker than for mothers (Kramer 1987). Paternal height and weight have been directly associated with body proportions at birth, but only in very few studies (Lenner 1943, Kapoor et al. 1985, Godfrey et al. 1997). Fathers who themselves were lighter at birth have been shown to have lighter babies, although effects were again weaker than those of maternal birthweight and were only investigated in very few studies (Ramakrishnan et al. 1999). Godfrey et al. (1997) found that low birthweight fathers had short babies, a relationship that was stronger than that with mother's birthweight, although there was no relationship with the offspring's PI.



Genetic effects from both parents influence the growth potential of the fetus, which regulates its demand for nutrients. In addition, the father determines the sex of the fetus, which also has an effect on its growth potential; males are generally larger than females, although have less fat (Copper et al. 1993). The mother may 'constrain' the growth of her fetus, as she must consider her own health as well as that of her fetus, unlike the father. Several examples of this have been shown in animal experiments, for example Walton and Hammond (1938) crossbred Shire horses and Shetland ponies, and found the foals to be of a size proportional to the dam's breed rather than the sires or an intermediate. Other similar experiments on cattle (Joubert and Hammond 1958) and sheep (Starke et al. 1958) had similar findings. As the mother has both environmental and genetic influences on the growth of the fetus, whereas the father has mainly genetic influences, it is expected that maternal rather than paternal influences would be greater. Brooks et al. (1995) demonstrated that in babies born after ovum donation, birthweights were unrelated to the weight of the women who donated the eggs, but were strongly directly related to the weight of the recipient mother. Morton (1955) showed that among half siblings, those related to the mother had similar birthweights, while those related to the father were less correlated.



The interactions between maternal environmental factors plus genetic factors from both parents, particularly the father, determine the size of the placenta (Devriendt 2000). Some of the nutrients obtained from the mother are used within the placenta, although further nutrient production also takes place here before transportation to the fetus. The fetal genome sets the growth trajectory of the fetus that is regulated by hormones and growth factors, but this may then be altered by the supply of nutrients received. If the demand for nutrients is not met due to maternal factors or inadequate placental transportation, the fetus becomes undernourished. Adaptations to this situation include endocrine changes (increased cortisol and decreased insulin, insulin-like-growth-factor 1 and growth hormone) and metabolic changes (increased amino acid

and lactate oxidation and decreased glucose oxidation) within the fetus. Blood flow may be redistributed, causing the fetus to suffer from hypoxaemia.

1.3.3 Timing of undernutrition

A fetus may become undernourished at any time during gestation, and this may coincide with critical periods of development for specific tissues, so that their growth is permanently impaired. Hence, undernutrition at different stages of gestation results in different types of growth retardation at birth. These have traditionally been summarised as the following groups (Kleine et al. 1989), although there may be overlap between them:

- Proportionately small neonate

Undernutrition in early gestation allows the fetus to reduce its demand for nutrients and establish a low trajectory of growth with reduced cell division, protecting itself from relative undernutrition in later gestation

- Stunted neonate

Undernutrition in mid gestation, so head size has been established, and continues to grow at the expense of the trunk. As it is too early for muscle and fat development, the neonate does not appear wasted

- Wasted neonate

Undernutrition in late gestation, so normal head size and length has been established, but the fetus then fails to gain subcutaneous fat. If undernutrition occurred early in the third trimester, the neonate would also be muscle depleted.

Proportionately small neonates are more common in developing countries, while growth retarded neonates in developed countries are more likely to be stunted or wasted (Kleine et al. 1989).

1.4 Hypothesis

1.4.1 Rationale

Evidence has been presented demonstrating the link between small size at birth and CHD and its associated disorders in later life. Hence it is important to understand the determinants of fetal growth. Geographical variations in neonatal phenotype are known to exist but have not been well documented, so a range of populations are required to investigate the determinants of fetal growth.

It has been well established that maternal size and body composition partly determine neonatal phenotypes. However, most studies relating the size of the mother to her baby considered only maternal height and weight, and their effects on neonatal birthweight. Many of these did not restrict to liveborn, singleton, term neonates, so may have been investigating prematurity rather than reduced fetal growth. Also, they may not have controlled adequately for confounders, or may have used inappropriate statistical techniques. Therefore, a clearer understanding of maternal-neonatal relationships is required, which may guide policy on recommendations regarding the ideal maternal body composition for pregnancy.

The role of the size and shape of the father is also of interest, as any relationships that exist between paternal and neonatal phenotypes that are independent of maternal phenotype must have a genetic basis. This contrasts with any relationships that exist between maternal and neonatal phenotypes, which may be a result of environmental factors, genetics or both. Very few studies have investigated this issue.

Relationships between size and body proportions at birth and cardiovascular disease in later life have been inconsistent across populations, with the exception of birthweight. Hence, possible reasons for differences in these relationships are of interest, and these may include geographical variation in size and shape of babies and also their mothers.

1.4.2 Objectives

The main objectives of this thesis were to:

- characterise geographical differences in neonatal and maternal phenotype within and between countries
- compare relationships between neonatal phenotype and maternal size and body composition in different populations
- establish the extent to which geographical differences in neonatal phenotype can be explained by differences in maternal size and body composition
- investigate the role of paternal size and body composition in determining neonatal phenotype
- examine to what extent geographical differences in neonatal phenotype explain differences in levels of blood pressure in later life, and also in their relationships with size at birth.

1.4.3 Approach

A number of datasets containing anthropometric measurements were available within the Medical Research Council Environmental Epidemiology Unit (MRC EEU) due to extensive collaboration with other investigators. These were used to fulfil the above objectives, ensuring that analyses on each dataset were as comparable as possible. Standard methods of analyses were used, as well as more novel statistical techniques.

2 Methods

2.1 Selection of datasets

Data from projects being carried out in collaboration with the MRC EEU, based on normal populations, and containing neonatal and maternal anthropometric measurements were considered for inclusion into the study. In some datasets paternal anthropometry, and measurements of blood pressure in childhood or adulthood were also recorded. In order to represent as many different ethnic groups as possible, areas covered included:

- UK — Southampton - four datasets (Godfrey et al. 1996a, Godfrey et al. 1998, Dewar et al. 1987, Wheeler et al. 1998)
  Preston (Barker et al. 1990)
  Sheffield (Barker et al. 1993a)
  Farnborough (de Swiet et al. 1980)
  Isle of Man (Lee 2000)
  Aberdeen (Campbell et al. 1996)
- Finland — Helsinki (Forsen et al. 1997)
- India — Mysore - two datasets (Stein et al. 1996, Hill 2000)
  Pune - two datasets (Yajnik et al. (2002), Yajnik et al. in press)
- Sri Lanka — Kandy (Lovel 1996)
- China — Beijing (Mi et al. 2000)
- Congo — Kasaji (Newby 2000)
- Nigeria — Imesi (Morley et al. 1964)
- Jamaica — Kingston - two datasets (Thame at al. 2000, Landman and Hall 1983).

For some populations, more than one dataset was included. This was due to one or more of the following reasons: different neonatal and/or maternal measurements were recorded, different settings were used such as urban or rural, different eligibility criteria were used, or sample size was small in a dataset which included detailed anthropometry and larger in a dataset containing less information so both were required.

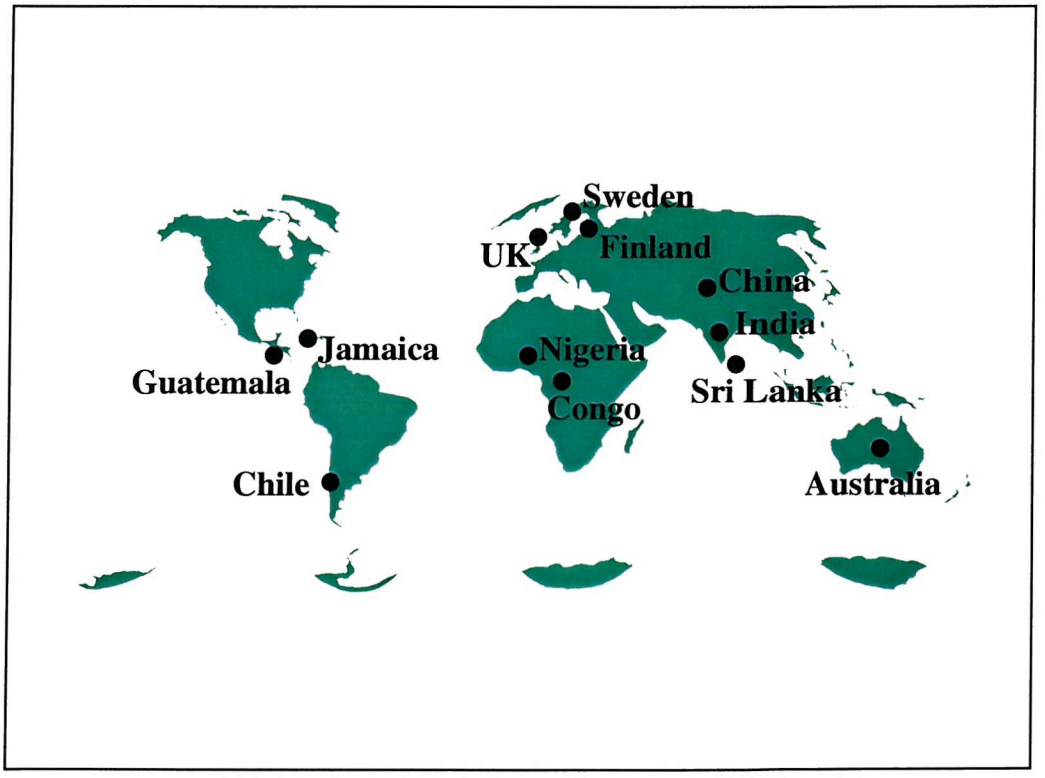
In addition, seven datasets from the World Health Organisation (WHO) were included, which were all based on a common protocol (Law et al. 2000):

- Sweden Uppsala
- Australia Sydney and Melbourne
- Chile Santiago
- Guatemala Guatemala City
- India New Delhi
- China Chengdu
- Nigeria Sagamu.

This enabled the consistency of some of the findings in the main study to be investigated using good quality data. It also allowed four new populations to be studied.

Figure 2.1 shows the locations of the 20 datasets in the main study and the seven in the WHO study.

Figure 2.1 Map illustrating location of datasets



2.2 Designs of datasets

Table 2.1 contains information on the designs used for each of the datasets. Shaded rows refer to prospective datasets in this table and all those that follow throughout the chapter.

Table 2.1 Dataset designs

Dataset	Prospective /retrospective	Setting	Rural /urban	Year of birth	Eligibility criteria Maternal	Neonatal	Source of data
Southampton 1	Prospective	Princess Anne Maternity Hospital, Southampton, UK	Urban	1992-93	< 17 weeks gestation White Caucasian Aged > 15 Non-diabetic	Singleton	Obstetric records Clinic forms Questionnaire
Southampton 2	Prospective	Princess Anne Maternity Hospital, Southampton, UK	Urban	1994-96	< 17 weeks gestation Known menstrual dates White Caucasian Aged > 15 Non-diabetic	Singleton	Obstetric records Clinic forms Questionnaire
Southampton 3	Prospective	Princess Anne Maternity Hospital, Southampton, UK	Urban	1987	Delivered*	Born during weekday Singleton Healthy	Obstetric records Clinic forms
Southampton 4	Prospective	Princess Anne Maternity Hospital, Southampton, UK	Urban	1985	Delivered* Caucasian Non-diabetic	Singleton Term Healthy	Obstetric records Clinic forms Questionnaire
Preston	Retrospective	Sharoe Green Hospital, Preston, UK	Urban	1935-43	Married	Liveborn Singleton	Obstetric records Clinic forms**
Sheffield	Retrospective	Jessop Hospital for Women, Sheffield, UK	Urban	1907-30		Liveborn Singleton	Obstetric records Clinic forms**
Farnborough	Prospective	Farnborough Hospital, Farnborough, Kent, UK	Urban	1975-77		Liveborn Singleton Term	Clinic forms Questionnaire Obstetric records
Isle of Man	Prospective	Nobles Isle of Man Hospital, Isle of Man, UK	Urban	1991-92	Delivered* Primagravida		Obstetric records Clinic forms Questionnaire
Aberdeen	Retrospective	Aberdeen Maternity Hospital, Aberdeen, Scotland,	Urban	1948-54	Married Primagravida		Obstetric records Clinic forms**
Helsinki	Retrospective	Helsinki University Central Hospital, Helsinki, Finland	Urban	1924-33			Obstetric records

* i.e. mothers were recruited after delivery as opposed to pre or during pregnancy

** for follow-up in childhood or adulthood only

Dataset	Prospective /retrospective	Setting	Rural /urban	Year of birth	Eligibility criteria Maternal	Neonatal	Source of data
Mysore 1	Retrospective	Holdsworth Memorial Hospital, Mysore, South India	Urban	1938-95		Liveborn	Obstetric records Clinic forms**
Mysore 2	Prospective	Holdsworth Memorial Hospital, Mysore, South India	Urban	1997-98	< 28 weeks gestation	Singleton	Clinic forms
Pune 1	Prospective	6 villages, 50km from Pune, South India	Rural	1994-96	Non-pregnant Aged 15 – 40 Married		Clinic forms
Pune 2	Prospective	King Edward Memorial Hospital, Pune, South India	Urban	1998	Delivered*	Singleton	Clinic forms
Kandy	Prospective	Kandy Hospital, Kandy, Sri Lanka	Urban	1985	Pregnant		Clinic forms Obstetric records
Beijing	Retrospective	Peking Union Medical College Hospital, Beijing, China	Urban	1948-54			Obstetric records Clinic forms**
Kasaji	Prospective	Kasaji Hospital, Congo, Central Africa	Rural	1995-98	Pregnant	Singleton	Clinic forms
Imesi	Prospective	Imesi village, West Nigeria	Rural	1957-58	< 24 weeks gestation	Singleton Term	Obstetric records
Kingston 1	Prospective	University Hospital of the West Indies, Kingston, Jamaica	Urban	1993-96	Booked in 1st trimester Known menstrual dates Aged 15 – 40 Healthy	Liveborn Singleton	Clinic forms
Kingston 2	Prospective	University Hospital of the West Indies, Kingston, Jamaica	Urban	1979-81	Booked in 1st trimester Aged 16 – 45 Healthy	Liveborn Singleton	Clinic forms

* i.e mothers were recruited after delivery as opposed to pre or during pregnancy

** for follow-up in childhood or adulthood only

Dataset	Prospective /retrospective	Setting	Rural /urban	Year of birth	Eligibility criteria Maternal	Neonatal	Source of data
WHO Sweden	Prospective	Uppsala University Hospital, Sweden	Urban	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy Literate	Singleton Term Healthy Not low birthweight	Clinic forms
WHO Australia	Prospective	Melbourne and Sydney, Australia	Urban	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy Literate	Singleton Term Healthy Not low birthweight	Clinic forms
WHO Chile	Prospective	Hospital Barros Luco, Santiago, Chile	Urban	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy Literate	Singleton Term Healthy Not low birthweight	Clinic forms
WHO Guatemala	Prospective	Instituto de Nutrition de Centro America and Panama, Guatemala City, Guatemala	Urban/rural	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy Literate	Singleton Term Healthy Not low birthweight	Clinic forms
WHO India	Prospective	National Institute of Health and Family Welfare, New Delorth India	Urban	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy Literate	Singleton Term Healthy Not low birthweight	Clinic forms
WHO China	Prospective	5 rural township areas, Pengxian County, 60km from Chengdu, China	Rural	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy Literate	Singleton Term Healthy Not low birthweight	Clinic forms
WHO Nigeria	Prospective	Ogun State University Teaching Hospital, Sagamu, Nigeria	Urban	1989-92	Delivered and intending to breastfeed Aged 20-37 Multiparous (previously breast fed) Healthy, literate	Singleton Term Healthy Not low birthweight	Clinic forms

2.2.1 Prospective vs retrospective

The designs of the datasets could be divided into two categories – those collected prospectively (subjects recruited at or before birth) and those collected retrospectively (subjects recruited in childhood or adulthood).

Prospective datasets

Southampton 1, Southampton 2, Mysore 2, Pune 1, Kasaji (Congo), Kingston 1 and Kingston 2 all involved detailed monitoring of mothers during pregnancy to investigate maternal determinants of birth size. In addition, both of the Kingston datasets followed subjects through childhood to study blood pressure levels. Southampton 3 was collected to characterise neonatal size and shape at birth, while Southampton 4 was set up to investigate the relationship between size at birth and childhood fingerprint patterns, which are known to be associated with adult hypertension. The Isle of Man dataset was collected to investigate the determinants of blood pressure and fibrinogen in neonates. The Farnborough data were collected to establish British standards for childhood blood pressure, although information on size at birth was also recorded.

In Pune 2, factors associated with umbilical cord blood measurements were of interest. The Kandy dataset was a pilot study for the United Nations Children's Fund to identify health issues requiring further attention in Sri Lanka. The dataset from Imesi (Nigeria) was set up to investigate causes of childhood illnesses, although there was also a controlled trial of pyrimethamine to suppress malaria in progress. Mothers who received this drug were not excluded from the current study as there were no significant differences between their offspring's birth measurements and those of mothers who had not received the drug, and also chloroquine sulphate was given to any mother who reported a fever, so in effect all were treated for malaria.

The data from the seven WHO centres were part of a study co-ordinated by the WHO Special Programme on Human Reproduction, which aimed to examine differences in duration of lactational amenorrhoea in relation to breastfeeding practises. In addition, subjects from some centres had their blood pressures measured in childhood.

Retrospective datasets

Preston, Sheffield, Helsinki, Mysore 1 and Beijing were based on routinely collected clinical data from obstetric records. These had later been used to investigate size at birth and cardiovascular disease and its risk factors in subjects who had been traced as children or adults. In Aberdeen, the primary aim was to look at relationships between size at birth based on obstetric records, and disease in adulthood, although nutrition in pregnancy was also recorded.

2.2.2 Settings

Further information was obtained on the settings for each dataset. This included the contribution of the hospitals to health care provision for the area and the proportion of home births, and also the circumstances of the women who gave birth in each population during the study periods. Unfortunately this type of information was not available in some cases.

At the start of the century, most births in England and Wales took place at home. In the 1920s, the proportion of home births was approximately 85%, which fell to just under 50% in the 1940s. This decreasing trend continued, so that by the 1990s less than 2% of women gave birth at home, although there has been a very small increase during the last ten years (Macfarlane and Mugford 2000). None of the UK datasets included home births.

The four Southampton datasets were collected in the Princess Anne Hospital, the only National Health Service maternity hospital in the city. The social class distribution of the women attending this hospital was similar to that of England and Wales. The Sharoe Green Hospital, used for the Preston dataset was one of several hospitals in the area where women may have delivered, as was the Jessop Hospital for women used for the Sheffield dataset. The Farnborough Hospital was the only hospital with maternity facilities in Kent, while most women on the Isle of Man gave birth at the Nobles Hospital. Aberdeen Maternity hospital was one of many hospitals in the city, although 90% of first pregnancies occurred there. In Helsinki, 60% of all births in the city took place at the University Hospital. Hence, datasets from Southampton, Farnborough and the Isle of Man were expected to be highly representative of each of the populations, while those in Preston and Sheffield, and to a lesser extent Aberdeen and Helsinki may have been less representative.

Both of the Mysore datasets were collected from the Holdsworth Memorial Hospital (HMH). This was one of three main hospitals offering obstetric care in the city in the first half of last century. The number of hospitals in the city grew rapidly, and only approximately 20% of all hospital deliveries took place at HMH during the last few years. The proportion of home births was high, although reduced considerably over the years, and as the datasets only included hospital births, mothers were more likely to have been at a higher risk of pregnancy or delivery problems. HMH was situated in a poor, overcrowded area of the city, although there was no extreme poverty. The poorer women delivered there as treatment was free, although fee-paying women also used the hospital due to its good reputation, so there was a range of mainly middle and lower social classes. Those paying fees were more likely to have received antenatal care and maybe had more detailed anthropometric measurements, while the poorer mothers probably only attended at delivery. The population in Mysore was relatively stable during the study periods.

The King Edward Memorial (KEM) Hospital, the setting for the Pune 2 dataset was one of several hospitals in the city with maternity facilities, although there were many home births. Both paying and non-paying women delivered at the hospital. The six rural villages that were used for the Pune 1 dataset had access to a community healthcare programme organised by KEM Hospital, although many births took place at home (included in the dataset). The area was prone to droughts, few were educated, and the main occupation was farming.

In Sri Lanka, more than 75% of births took place in hospital, so this was one of the few developing countries where a hospital based study could obtain a group of people fairly representative of those having babies. The women attending the Kandy Hospital were Sinhala, and from a range of social classes, although the more affluent used the nearby teaching hospital or private clinics.

Peking Union Medical College was one of several health centres in Beijing, and there were also many home births (excluded from the dataset). Both paying and non-paying women delivered here, but they were typically of higher education and income than average. Communism was established in China at the start of data collection, so the women would have experienced many changes over the study period. This included new nation-wide health campaigns, and a change in the marriage law that increased the legal age of marriage from 15 to 20 years.

The Kasaji Hospital in the Congo was the only referral hospital in a radius of 130km, so was attended by both local women and those from further afield, although there were also many home births (excluded from the dataset). Patients paid for their treatment, although were heavily subsidised by gifts from Christian churches, as this was a mission hospital. The people were generally poor, and the main occupation was farming.

The rural village of Imesi with a population of just under 5000 was the setting for the Nigeria dataset. Births took place either at a clinic set up by the Wesley Guild Hospital in the town of Illesha that was 25 miles away, or at home, and the dataset included both of these circumstances. The community was relatively stable, the majority of people were Yoruba, and farming was the chief occupation.

In Jamaica, the population is primarily of African descent. Both of the Kingston datasets were based at the University Hospital of the West Indies, where over 80% of births on the island took place. The intensive care neonatal unit there was also used as a referral centre. Middle class fee-paying women delivered there, as well as women from the lower classes who lived in the poorer suburbs where homes were overcrowded with poor amenities, but were not the poorest in Kingston. Mothers in the Kingston 2 dataset were recruited from public and private clinics to obtain a wider range of social classes.

The WHO Sweden dataset was collected in Uppsala, where all births took place in hospital. The mothers attending the Uppsala University Hospital in Sweden were all from the city, and were likely to have been receiving optimal nourishment. For the WHO Australia dataset, approximately half the mother-baby pairs were from each of Melbourne and Sydney. Almost all deliveries took place in hospital in these areas. The WHO Chile dataset included mothers from low income groups in Southern Santiago. Many were migrant, and lived in overcrowded housing with no luxury goods but had reasonable sanitary facilities. In this population, 97% of births were in some form of institution. The women who attended the Instituto de Nutrition de Centro America and Panama in Guatemala City were from the urban area and also the accessible rural areas. The WHO India data were collected from three areas in New Delhi, all within 10km of the National Institute of Health and Family Welfare. In total, approximately 90% were urban poor (20% below the poverty line), and 10% were urban privileged. The population was relatively stable. The proportion of deliveries that were in an institution as opposed to at home in these areas ranged from 60% to 90%. In the rural areas used for the WHO China

dataset, the majority of births were at home, and these were included in the study. Mothers within 20km of the Ogun State University Teaching Hospital in Sagamu were recruited for the WHO Nigeria dataset. Sagamu was one of the main towns in the area, with several health facilities used by 89% of the population. The women were mainly Yoruba, lived in fair housing with basic facilities, and were from low income groups.

2.2.3 Year of birth

The year of birth of the neonates ranged from 1907 to 1998. All the prospective datasets were based on neonates who were born in the latter half of the century, and covered relatively short periods. The retrospective datasets were based on earlier years of birth, and covered longer periods.

2.2.4 Eligibility criteria

Maternal eligibility criteria were based on ethnic group, age, parity, medical history and/or marital status. Some of the populations were highly selective. For example, in some of the Southampton and Jamaican datasets, women had to have booked early and/or known their menstrual dates, so were likely to be more motivated, or to have had a history of previous pregnancy or delivery complications. Also, in the WHO datasets the women had to be literate, so were likely to have been from the more educated or affluent areas of the populations studied.

To be eligible for some of the datasets, neonates had to be liveborn, singleton and/or full term births. In addition, in the WHO datasets low birthweight babies were not recruited. This was defined to be less than 2500g (2000g in India), or below the 10^{th} centile of the local reference standard.

2.2.5 Source of data

Datasets were created from clinic forms, questionnaires, obstetric records or a combination of these. Clinic forms contained measurements of specific interest made only on women (before or during pregnancy) and neonates that were included in the datasets. They were also used to record blood pressure measurements in childhood or adulthood in some datasets. Questionnaires contained self-reported values, again only on those

included in the datasets. Obstetric records contained routinely recorded information for all births in the hospital. Examples of a clinic form from Mysore 2 (prospective dataset), and an obstetric record from Mysore 1 (retrospective dataset) are shown in Figures 2.2a and 2.2b respectively.

Figure 2.2a Clinic form for Mysore 2

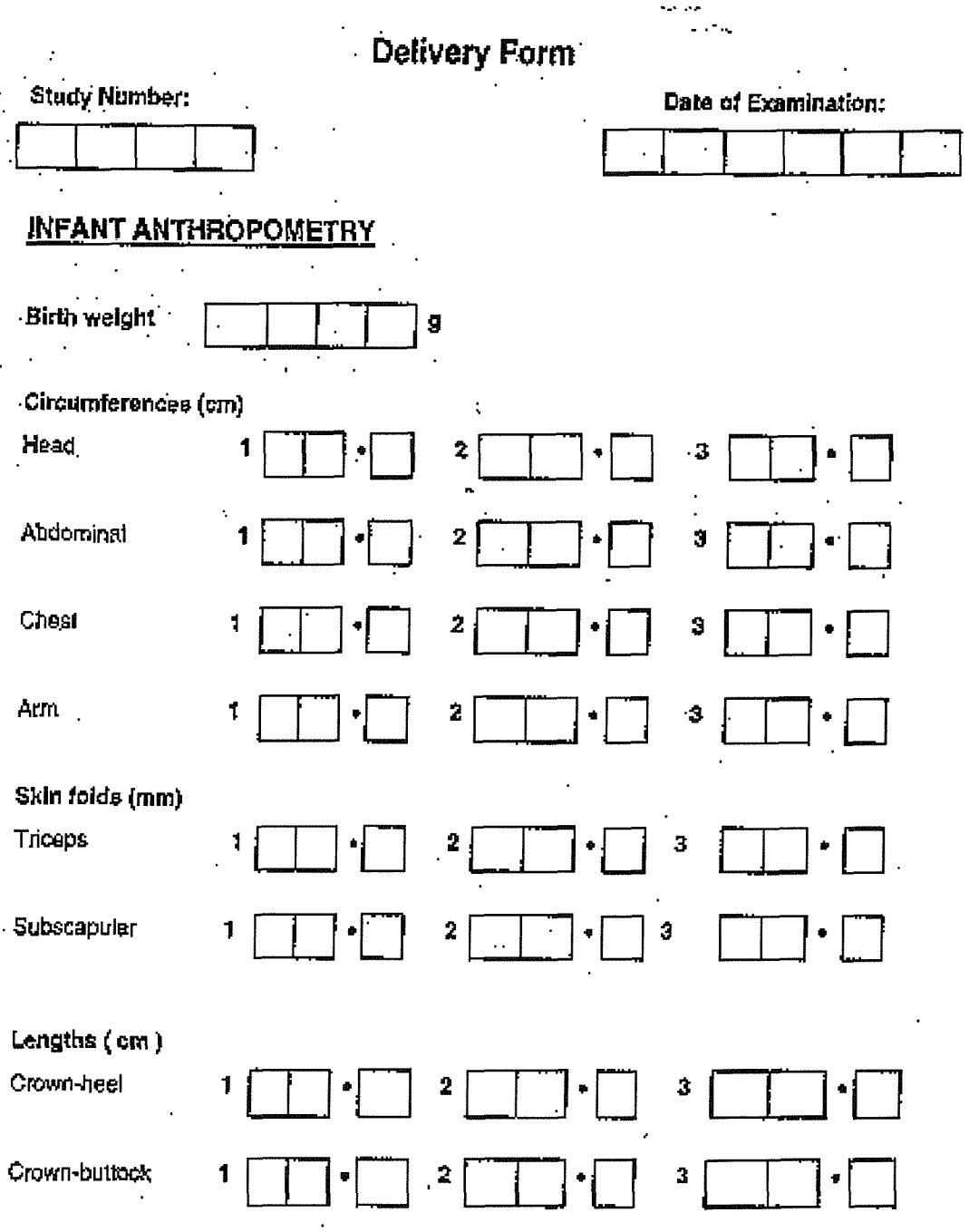
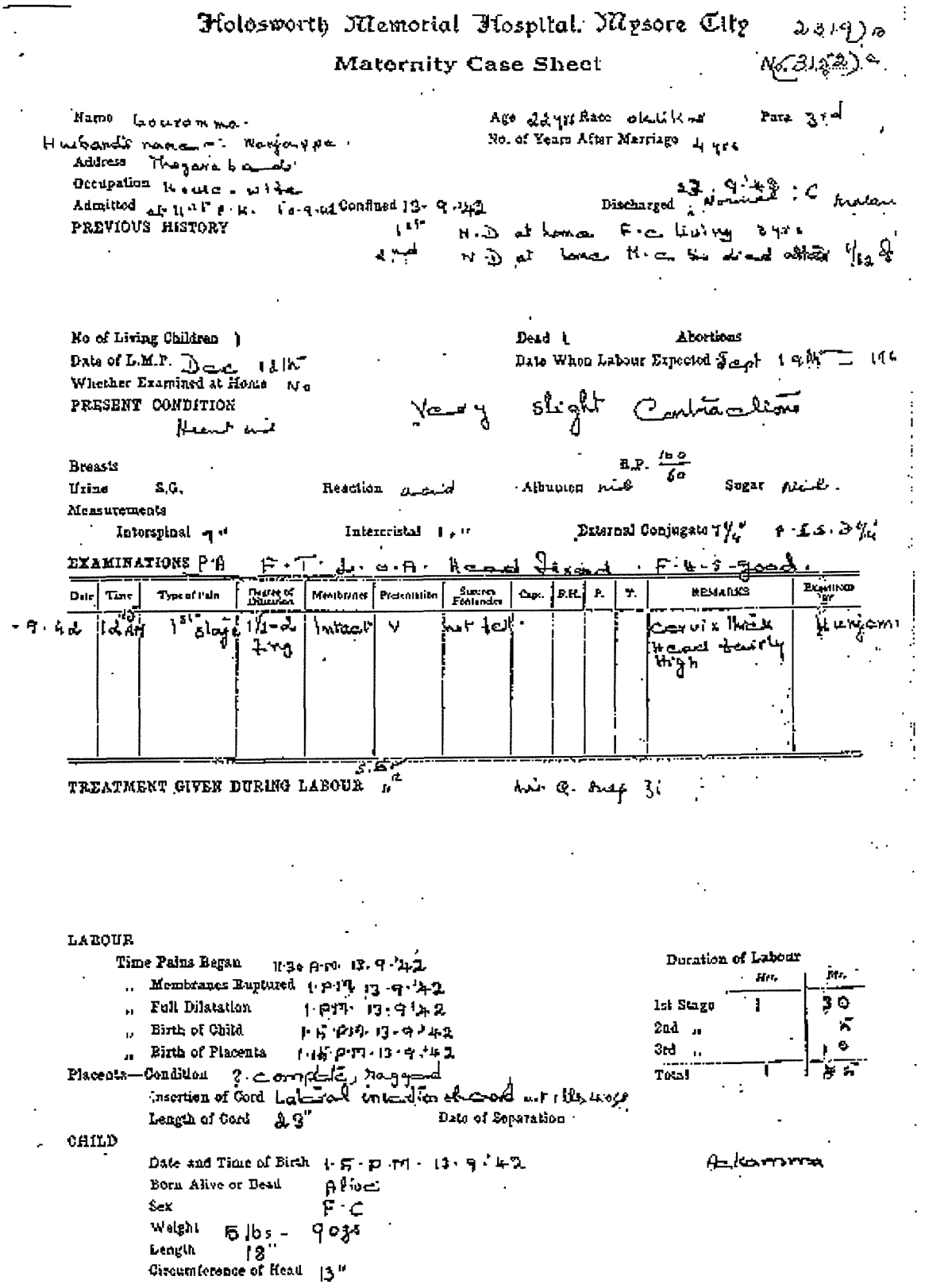


Figure 2.2b Obstetric record for Mysore 1



Holesworth Memorial Hospital. Mysore City

Maternity Case Sheet

Name Gowramma. Age 22 yrs Race Hindu Para 3rd

Husband's name Nanjappa. No. of Years After Marriage 4 yrs

Address Nagara Mohalla

Occupation House wife

Admitted at 11 A.M. 12-9-42 Confined 13-9-42 Discharged 23.9.42 : C Improved

PREVIOUS HISTORY 1st N.D at home F.C living 3 yrs

2nd N.D at home M.C She died after 4½ days

No of Living Children 1 Dead 1 Abortions

Date of L.M.P. Dec 18th Date When Labour Expected Sept 19th — 1942

Whether Examined at Home No

PRESENT CONDITION Very slight Contractions

Heart nil

Breasts

Urine S.G. Reaction acid Albumen nil Sugar nil.

B.P. 120/60

Measurements

Interspinal 9" Intercristal 11" External Conjugate 7¼" P.S. 3¼"

EXAMINATIONS P.V. F.T. d. c.A. Head fixed. F.H.S. good.

Date	Time	Type of Pain	Degree of Dilatation	Membranes	Presentation	Sutures Fontanelles	Caput	B.H.	P.	V.	REMARKS	Examined by
9.9.42	10 AM	1st stage	1½-2 fingers	Intact	V	not felt					Cervix thick Head fairly high	Lingam

TREATMENT GIVEN DURING LABOUR Nil Q. Aug 31

LABOUR

Time Pains Began 11.30 A.M. 13.9.42

" Membranes Ruptured 1 P.M. 13-9-42

" Full Dilatation 1 P.M. 13-9-42

" Birth of Child 1.15 P.M. 13-9-42

" Birth of Placenta 1.45 P.M. 13-9-42

Placenta—Condition ? complete, Ragged

Insertion of Cord Lateral inside sheath of membranes

Length of Cord 23" Date of Separation

Duration of Labour	Hrs.	Mts.
1st Stage	1	30
2nd "		15
3rd "		10
Total	1	55

CHILD

Date and Time of Birth 1.55 P.M. 13.9.42 Alamma

Born Alive or Dead Alive

Sex F.C

Weight 5 lbs - 90 zs

Length 18"

Circumference of Head 13"

2.3 Numbers in datasets

Table 2.2 shows the numbers in each dataset, with details of exclusions.

Table 2.2 Numbers in datasets

Dataset	Original Eligible	Data collected	Current study Liveborn	Singleton	Term	Neonatal anthropometry*
Southampton 1, UK	667	608	596	557	557	557
Southampton 2, UK	630	562	555	555	521	521
Southampton 3, UK	1071	390	390	390	377	377
Southampton 4, UK	Not known	102	102	102	102	102
Preston, UK	1298	1298	1298	1298	1044	1014
Sheffield, UK	8577	8577	8577	8577	4587	4418
Farnborough, UK	2088	1677	1677	1677	1677	1677
Isle of Man, UK	750	452	452	440	403	388
Aberdeen, UK	544	260	260	253	233	233
Helsinki, Finland	27068	7088	7088	7088	5989	5989
Mysore 1, India	57691	2676	2676	2673	1237	1237
Mysore 2, India	1235	676	662	662	597	597
Pune 1, India	2675 (1102 pregnancies)	773	756	753	633	633
Pune 2, India	471	362	346	346	278	269
Kandy, Sri Lanka	2304	506	470	457	455	455
Beijing, China	2954	2943	2864	2769	2509	2433
Kasaji, Congo	529	347	338	338	338	338
Imesi Nigeria	504	301	279	279	279	269
Kingston 1, Jamaica	712	561	561	561	490	490
Kingston 2, Jamaica	146	78	78	78	70	70
WHO Sweden		505	505	505	505	505
WHO Australia		623	623	623	623	622
WHO Chile		688	688	688	688	688
WHO Guatemala		686	686	686	299	294
WHO India		550	550	550	550	504
WHO China		541	541	541	541	541
WHO Nigeria		520	520	520	513	512

*recorded within 7 days of birth

The first two columns relate to the original data collection, although it was not possible to obtain the number of eligible neonates for the WHO datasets. Data were not collected from all eligible mothers usually because they refused to participate, or delivered outside the hospital. For some retrospective datasets, it was possible to include all births that occurred during the study periods, rather than just those that were traced and studied as children or adults. However, in Aberdeen, Helsinki and Mysore 1, it was only possible to obtain data on subjects who had been traced in later life. Hence only subjects still living in the relevant areas who gave consent were included. There was a large discrepancy between the number of eligible subjects and those for whom data were collected in Southampton 3 as recruitment took place during weekdays only, with limited time available in each week during the study period. In Kandy, only 23% of the births that took place in the hospital during the study period were included (convenience sample). If data were collected but neonatal sex was not recorded, exclusions were also made at this stage.

The final four columns refer to restrictions imposed for this study. Only live births were included, and neonates had to be singletons as multiple pregnancies suffer additional restrictions in intrauterine growth. Only those born at full term (at least 37 weeks) were included to ensure any low birthweights were due to failure to grow rather than prematurity. Any neonates with gestational ages greater than 44 weeks were excluded, as there were likely to have been errors in last menstrual period (LMP) dates. Hence the difference between the columns displaying the number of liveborns and the number of terms births may have included pre-terms, post-terms or those without gestation recorded. It is possible that the original data collection had already been restricted to singletons, livebirths and/or term births, depending on the eligibility criteria (see Table 2.1).

At least one neonatal anthropometric measurement was required for inclusion in the datasets. Measurements were restricted to those made within seven days of birth. There may have been some changes during this period, but these are expected to have been minimal, particularly for the skeleton. For example, Gerver and de Bruin (1996) found changes of just 2% in both length and head circumference. The only dataset affected by this was Imesi, where eight sets of measurements were recorded after seven days, one as late as 21 days. This was because many babies were born at home and brought into the clinic on the day of delivery for measurement, but this visit may have been delayed. If the time of measurement was not known for datasets that generally included this information, neonates were not excluded as this would have meant further loss of data, and the

problems encountered in Imesi were unlikely to have occurred elsewhere. For the WHO datasets, neonates were also excluded from the final column if their birthweight was less than 2500g for consistency within these seven populations.

There were further exclusions for analyses involving mothers, fathers, and blood pressure in childhood or adulthood, and details of these are given in the relevant chapters.

2.4 Anthropometric measurements

In general, if datasets were collected prospectively and anthropometric measurements recorded on clinic forms, more rigorous techniques were adopted than if the datasets were collected retrospectively, using obstetric records that were already in existence. Details of equipment and techniques were often unknown in the latter case.

For many of the prospective datasets, observers followed protocols, and had been trained through involvement in inter- and intra-observer tests of agreement and repeatability at the start and possibly throughout the data collection. Most data were collected by more than one observer either concurrently or in series. Only the Isle of Man data were collected entirely by a single individual. Measurements were often replicated two or three times on the same occasion, and the mean value calculated to increase accuracy. The degree of precision of measurement was also specified for some datasets, for example neonatal birthweight to the nearest 25g. A small number of the prospective datasets used questionnaires to obtain further information. Any anthropometric data from these would have been self-reported values and therefore less reliable.

For the retrospective datasets, measurements were made by midwives who had not received any specific training in addition to the standard job requirements. Only single values would have been recorded, and no degree of precision would have been specified.

The following descriptions of measurement techniques apply to those datasets where information was available, mainly prospective datasets.

2.4.1 Neonatal anthropometry

Table 2.3 shows the neonatal measurements that were available in each of the datasets.

Table 2.3 Neonatal measurements available in each dataset

Dataset	Birthweight	Placental weight	CH length	CR length	Head	Chest	Abdomen	MUAC	Triceps	Subscapular
Southampton 1, UK	✔	✔	✔	✔	✔		✔	✔		
Southampton 2, UK	✔	✔	✔	✔	✔		✔	✔		
Southampton 3, UK	✔	✔	✔		✔		✔	✔		✔
Southampton 4, UK	✔	✔	✔	✔	✔		✔	✔		
Preston, UK	✔	✔	✔		✔					
Sheffield, UK	✔	✔	✔		✔		✔			
Farnborough, UK	✔	✔	✔		✔					
Isle of Man, UK	✔	✔	✔		✔		✔			
Aberdeen, UK	✔	✔								
Helsinki, Finland	✔	✔	✔		✔					
Mysore 1, India	✔	✔	✔		✔					
Mysore 2, India	✔	✔	✔	✔	✔		✔	✔	✔	✔
Pune 1, India	✔	✔	✔		✔	✔	✔	✔	✔	✔
Pune 2, India	✔	✔	✔		✔	✔	✔	✔	✔	✔
Kandy, Sri Lanka	✔		✔		✔					
Beijing, China	✔	✔	✔	✔	✔					
Kasaji, Congo	✔	✔	✔		✔	✔		✔	✔	✔
Imesi Nigeria	✔	✔	✔		✔	✔				
Kingston 1, Jamaica	✔	✔	✔	✔	✔	✔	✔	✔		
Kingston 2, Jamaica	✔	✔	✔	✔	✔					
WHO Sweden	✔		✔		✔	✔				
WHO Australia	✔		✔		✔	✔				
WHO Chile	✔		✔		✔	✔				
WHO Guatemala	✔		✔		✔					
WHO India	✔		✔		✔	✔				
WHO China	✔		✔		✔	✔				
WHO Nigeria	✔		✔		✔	✔				

Birthweight and placental weight were measured using digital scales or beam balances. In some datasets, placentas were trimmed before weighing, which entailed removing the membranes and umbilical cord. However, in others, usually those based on obstetric records, placentas were weighed untrimmed. Chapter 3 investigates this issue further.

Crown-heel (CH) and crown-rump (CR) lengths were measured using a neonatal stadiometer, neonatometer or rollametre in datasets based on clinic forms. In those based on obstetric records, length was likely to have been measured by holding the neonate up and using a tape measure, which may lead to overestimation of values.

Head circumference was taken as the maximum occipital-frontal circumference. Chest circumference was measured at the level of the nipple. Abdominal circumference was measured at the level of the xiphisternum in all datasets except those from Pune, where it was measured at the level of the umbilicus. Measurements at the xiphisternum were preferable as there would be less distortion by feeding, and also the xiphisternum is more in the region of the liver, which is the purpose of taking this measurement. A small study was undertaken at the KEM hospital in Pune where 50 neonates were measured at both the xiphisternum and umbilicus. This enabled the umbilicus measurements to be adjusted to the level of the xiphisternum using regression in both the main Pune datasets. Mid-upper-arm circumference (MUAC) was measured mid-way between the acromion and olecranon. For all circumferences, plastic, paper or fibreglass tapes were used. In Kasaji, an insertion tape was used, so the measurer may have pulled tighter, resulting in smaller values.

Skinfolds were measured at two sites, the triceps and subscapular. These were either measured by Harpenden 'John Bull' callipers with external springs or Holtain callipers with an internal spring mechanism. There is no universal measurement technique, and there were variations in side of body used (this also applied to MUAC), the location of measurement point, picking up the skinfold, positioning the callipers and timing of the reading. For example, in Southampton and India readings were taken six seconds after the callipers had been applied, while in Kasaji, readings were not taken until the needle on the dial was steady, normally several seconds after application of the calliper.

The only other measurement recorded was calf circumference, but as this was only available in Kasaji, it was not used for analysis.

2.4.2 Maternal anthropometry

The maternal measurements available in each dataset are shown in Table 2.4. Only those recorded pre or during pregnancy were included, and further details of timepoints for measurements in each dataset are given later (Table 2.6).

Height was measured using a stadiometer, usually without shoes. Weight was measured using either digital scales or beam balances, and there may have been inconsistencies across datasets regarding clothes and shoes worn during measurements. Head and mid-upper-arm circumferences were measured using the same techniques as for neonates. Metal, steel or fibreglass tapes were used. Skinfolds were also measured in the same way as the neonates. Biceps and suprailiac were recorded in addition. In Southampton 1 both upper and lower suprailiac measurements were recorded, while the lower only was recorded in Southampton 4, and the upper only in Mysore 2 and Pune 1.

Maternal birthweight was available for some datasets, although in most cases was self-reported. There was no information available on whether the mothers were singletons, or lengths of their gestations. Hence there are likely to have been some pre-terms included.

Some available anthropometric measures have not been considered. Pelvic measurements were recorded in Preston, Sheffield, Helsinki, Mysore 1, Mysore 2, Beijing and Kasaji. However, these were not included in analysis as measurements have been shown to bear little relation to the actual size of the pelvis (Holland and Brews Manual of Obstetrics 1980), and also are a composite measure of fat and skeleton, and for both of these, superior measurements were available. This meant that Preston and Sheffield did not satisfy the entry criteria to the main study as datasets had to include maternal measurements. However, as they provided useful information on neonatal phenotypes, they were not excluded.

Abdominal, mid-thigh, waist and hip circumference had each been recorded in a maximum of two datasets, so were not included in analysis.

Table 2.4 Maternal measurements available in each dataset

Dataset	Height	Weight	Head	MUAC	Triceps	Biceps	Subscapular	Supralliac	Birthweight
Southampton 1, UK	✔	✔	✔	✔					✔*
Southampton 2, UK	✔	✔	✔	✔	✔	✔	✔	✔	✔*
Southampton 3, UK	✔	✔							
Southampton 4, UK	✔*	✔							✔*
Preston, UK									
Sheffield, UK									
Farnborough, UK	✔	✔							
Isle of Man, UK	✔	✔							✔*
Aberdeen, UK	✔	✔							
Helsinki, Finland	✔	✔							
Mysore 1, India	✔	✔							✔
Mysore 2, India	✔	✔	✔	✔	✔	✔	✔	✔	✔
Pune 1, India	✔	✔	✔	✔	✔	✔	✔	✔	
Pune 2, India	✔		✔						
Kandy, Sri Lanka	✔	✔		✔					
Beijing, China	✔	✔							
Kasaji, Congo	✔	✔		✔	✔				
Imesi Nigeria	✔	✔							
Kingston 1, Jamaica	✔	✔			✔				
Kingston 2, Jamaica	✔	✔		✔	✔	✔	✔	✔	
7 WHO datasets	✔								

*self-reported

2.4.3 Paternal anthropometry

Table 2.5 shows which datasets included measurements of height and weight in fathers.

Table 2.5 Paternal measurements available in each dataset

Dataset	Height	Weight
Southampton 1, UK	✔*	
Southampton 2, UK	✔*	
Southampton 4, UK	✔*	
Farnborough, UK		✔
Isle of Man, UK	✔*	
Mysore 1, India	✔	✔
Mysore 2, India	✔	✔
Pune 1, India	✔	✔
Kasaji, Congo	✔	✔
Imesi, Nigeria	✔	✔

*self-reported

In addition, head and mid-upper-arm circumferences and also skinfolds were recorded, but each only in one dataset, so were not included in analysis. Waist and hip circumferences were each measured in two datasets, but were not included as comparable measurements were not available for mothers.

2.4.4 Confounders

When considering relationships between maternal and neonatal anthropometric measurements, gestational duration, parity, maternal age at delivery, and sex of the baby were considered as potential confounders. It was not possible to include any other possible confounders due to unavailability of information in some datasets.

Gestational age

In most cases, the reported LMP was used to calculate gestational age at delivery, and also the gestation of any measurements made during pregnancy. In some datasets scans were used instead, if the LMP was unknown, or if there was more than a two or three week discrepancy. In the Isle of Man dataset, clinical examinations of the newborn (Dubowitz, 1970) were undertaken if no other information was available. In Farnborough and the seven WHO datasets gestation was only recorded in weeks, assumed to be complete, so was converted to days through multiplying by 7 and adding 3.5.

In Kandy, Narayanan scoring (Narayanan and Gujral 1981, Narayanan et al. 1981, Narayanan et al. 1982, Lovel 1996) which is a simplified version of the Dubowitz method was used, as menstrual histories were very unreliable. Some women were still lactating and had not menstruated since their last delivery, while others had no idea and just guessed to satisfy the midwife (Lovel, personal communication). Although in some of the other datasets, especially those from developing countries, LMP dates were unreliable, they had to be used as no other option was available. In Imesi, gestation could not be calculated as LMP was not recorded, and no clinical examinations had been undertaken. However, midwives identified pre-terms based on physical appearance, so these could be excluded.

Parity

Parity was defined to be the number of previous births that reached viability. If this information was not available, a substitute was used such as the number of previous labours (Preston and Sheffield), or the number of previous liveborns plus stillborns (Kandy and Kasaji). In the Isle of Man and Aberdeen datasets, all mothers were primiparous, while in the seven WHO datasets all mothers were multiparous.

Maternal age

Maternal age was calculated from maternal and neonatal dates of birth truncated to whole years where possible. Otherwise the age recorded closest to the delivery was used, although this may have been as early as booking. This was common in the developing countries, as exact date of birth was often unknown. For example, maternal age in Imesi was estimated using local or national events.

2.4 Blood pressure measurements

Blood pressure measurements in childhood or adult life were available in Preston, Sheffield, Farnborough, Aberdeen, Mysore, Beijing, Kingston and five of the WHO datasets. Blood pressure varies substantially throughout the day, and McAlister and Straus (2001) have reviewed additional factors that may interfere with the accuracy of blood pressure measurements. These include the 'white coat effect', whereby readings are often higher than their true values due to the anxiety associated with a clinic setting. However, in each dataset, measurements were made as rigorously as possible. All blood pressure

measurements were collected by trained observers, who were unaware of the subjects' birth measurements. Two or three readings were taken on the same occasion, and the mean value calculated to increase accuracy. Most studies used an automated recorder (Dinamap or Omron), although in Kingston 1 an oscillometric sphygmomanometer was used. Wattigney et al. (1996) found that systolic blood pressure was comparable between these two devices in children, and Friedman (1997) argued that both methods were acceptable in adults. Protocols varied across datasets with respect to which arm was used for measurements, and no details were given regarding the level of the arm. Most specified that the appropriate cuff size was selected. Readings were taken when subjects were sitting down, and in most of the datasets, they had been rested for at least five minutes.

The subjects' heights and weights were also recorded by the observer at the time of blood pressure measurement. Stadiometers were used for height, and portable scales for weight. In general, height was recorded two or three times and the mean value calculated, while weight was only measured once.

2.6 Statistical methods

2.6.1 Standardisation of maternal measurements at different timepoints

Maternal measurements were made before pregnancy, or at various times during pregnancy. Height and head should not change during pregnancy, so the time of measurement was less important for these variables. Height was measured on more than one occasion in Kingston 1, and for this dataset the mean value was used in analysis. The time of measurement does have an effect on measurements of weight, MUAC and skinfolds. The first column in Table 2.6 shows when weight was measured in each dataset (with ranges in brackets).

Table 2.6 Time of measurement for maternal weight

	Original measurements	Pre-pregnant	20 weeks	30 weeks	37 weeks
Southampton 1, UK	Pre, early, late pregnancy	✔*	Early (4-23 wks)**	Late (15-42 weeks)**	-
Southampton 2, UK	Pre-pregnant, 18 weeks, 28 weeks	✔*	18 week**	28 week**	-
Southampton 3, UK	Booking, 28-34 weeks, final before delivery		Booking (9-27 weeks)**	28-34 week*	Final before delivery**
Southampton 4, UK	Pre-pregnant, booking	✔*	-	Booking (6-20 weeks)*	-
Farnborough, UK	<= 21 antenatal		Interpolated (1-39 weeks)	Interpolated (1-41 wks)	Last antenatal**
Isle of Man, UK	Booking		-	Booking (1-36 weeks)**	-
Aberdeen, UK	<=16 antenatal		Interpolated (9-35 weeks)	Interpolated (17-36 weeks)	Last antenatal**
Helsinki, Finland	Admission to labour		-	-	Admission to labour**
Mysore 1, India	<= 11 antenatal, admission to labour		Interpolated (2-41 weeks)	Interpolated (9-41 weeks)	Last antenatal**
Mysore 2, India	28-32 weeks		-	28-32 weeks**	-
Pune 1, India	Pre-pregnant, 18, 28, 34 weeks, final before delivery	✔	18 week**	28 week**	Final before delivery**
Kandy, Sri Lanka	Booking		-	Booking (27-42 weeks)**	-
Beijing, China	<= 14 antenatal		Interpolated (6-42 weeks)	Interpolated (6-42 weeks)	Last antenatal**
Kasaji, Congo	<= 29 antenatal		Interpolated (8-37 weeks)	Interpolated (17-37 weeks)	Last antenatal**
Imesi, Nigeria	<= 11 antenatal		Interpolated (12-40 weeks)	Interpolated (21-40 weeks)	Last antenatal**
Kingston 1, Jamaica	Booking, 6 visits during pregnancy		Visit 4 (11-23 weeks)**	Visit 6 (21-33 weeks)**	Visit 7**
Kingston 2, Jamaica	Booking, 6 visits during pregnancy		Visit 2 (18-21 weeks)**	Visit 4 (29-31 weeks)**	Visit 6/5**

* self-reported

** adjusted using regression

Choice of timepoints

Standardisation methods were required to obtain a set of comparable weights from as many datasets as possible. Four timepoints were chosen, which were pre-pregnancy, 20, 30 and 37-weeks. Pre-pregnant measurements were the ideal as these were a true reflection of the mother's weight, but were not available in most datasets. 37-weeks was chosen to represent the final measurement before delivery, as the entry criteria to the main study required births to be at least as late as this. 20 and 30-weeks were chosen to use as much of the data as possible for datasets that included antenatal measurements, but without becoming too close to 37-weeks.

Datasets based on clinic forms

For datasets with weights recorded at specific timepoints, regression was used to adjust to the chosen values. No restrictions on time between actual measurement and chosen time were used for either 20 or 30-weeks, so as to make use of as much of the data as possible. For 37-weeks, the measurement had to be within four weeks of delivery so that the final weight before delivery was fairly represented.

Datasets based on obstetric records

For datasets with antenatal weights, the final weight, adjusted using regression was used to derive the 37-week measurements if it was within four weeks of delivery. In Imesi, although gestation was not recorded at delivery, estimates were made for the time of each antenatal measurement. Hence 37-week values based on the final antenatal weight were only derived in this dataset if the estimated gestation was within four weeks of 37-weeks, as it was known that all babies were born at term.

Interpolation was used to obtain weights at 20 and 30-weeks. Firstly, the appropriate serial weights were selected for each woman individually, so for 20-weeks, the closest values before and after 20 weeks were chosen. If both of these values existed, the weight at exactly 20-weeks could then be interpolated. Values may have been used to interpolate both the 20 and 30-week value, if the women only had one measurement recorded between these timepoints. Again, no restrictions were placed on time of measurement so as to make as much use of the available data as possible. This method assumed linear changes in weight over time. An alternative, more sophisticated method was also attempted (Royston 1991), whereby polynomial curves were fitted to the data and standard deviation scores used to interpolate appropriate weights. However, resulting values were

almost identical to those obtained from the simpler, quicker method described above, and so this was used in preference.

The final four columns of Table 2.6 show which standardised weights were available in each dataset. Similar methods were used to derive standardised measurements of MUAC and skinfolds, although these variables were recorded for fewer timepoints in fewer datasets.

2.6.2 Calculation of new variables

Neonatal variables

Leg length was calculated by subtracting CR length from CH length. Arm muscle area (AMA) was calculated using the following (Jelliffe and Jelliffe 1960):

$$\text{AMA}(\text{cm}^2) = \frac{(\text{MUAC} - \pi \times \text{triceps})^2}{4\pi} \qquad \text{with MUAC and triceps in cm.}$$

This formula was derived from geometry to calculate the inner area of the arm after the outside layer of fat had been removed. To calculate Ponderal index (Livi 1897), the following was used:

$$\text{PI}(\text{kg}/\text{m}^3) = \frac{\text{Birthweight}}{(\text{CHlength})^3} \qquad \text{with birthweight in kg and CH length in metres.}$$

Three ratio variables were calculated: head to CH length, head to abdomen and placental weight to birthweight.

Maternal and paternal variables

Body mass index (Quetelet 1869) was calculated at each timepoint using the following:

$$\text{BMI}(\text{kg}/\text{m}^2) = \frac{\text{Weight}}{(\text{Height})^2} \qquad \text{with weight in kg and height in metres.}$$

For mothers, AMA was calculated at each timepoint using the same formula as for neonates, but subtracting 6.5 from the resulting values. This adjustment factor (Heymsfield et al. 1982) was based on a comparison of computerised tomography scans with calculated AMA. It attempted to correct for overestimation of muscle area through inclusion of bone area, and also the assumption that the upper arm was circular. No comparable adjustment factor has been developed for neonates.

Table 2.7 shows which new variables were available in each dataset.

Table 2.7 Derived variables available in each dataset

Dataset	Neonatal						Maternal		Paternal
	Leg length	AMA	PI	Head/length	Head/abdomen	Placenta/birthweight	BMI	AMA	BMI
Southampton 1, UK	✔		✔	✔	✔	✔	✔		
Southampton 2, UK	✔		✔	✔	✔	✔	✔	✔	
Southampton 3, UK			✔	✔	✔	✔	✔		
Southampton 4, UK	✔		✔	✔	✔	✔	✔		
Preston, UK			✔	✔		✔			
Sheffield, UK			✔	✔	✔	✔			
Farnborough, UK			✔	✔		✔	✔		
Isle of Man, UK			✔	✔	✔	✔	✔		
Aberdeen, UK						✔	✔		
Helsinki, Finland			✔	✔		✔			
Mysore 1, India			✔	✔		✔	✔		✔
Mysore 2, India	✔	✔	✔	✔	✔	✔	✔	✔	✔
Pune 1, India		✔	✔	✔	✔	✔	✔	✔	✔
Pune 2, India		✔	✔	✔	✔	✔			
Kandy, Sri Lanka			✔	✔			✔		
Beijing, China	✔		✔	✔		✔	✔		
Kasaji, Congo		✔	✔	✔		✔	✔	✔	✔
Imesi Nigeria			✔	✔		✔	✔		✔
Kingston 1, Jamaica	✔		✔	✔	✔	✔	✔		
Kingston 2, Jamaica	✔		✔	✔		✔	✔	✔	
7 WHO datasets			✔	✔					

2.6.3 Data cleaning

In many of the datasets, variables were double-entered and discrepancies between the two entries corrected. Otherwise, data were only single-entered. All variables were converted to metric units if necessary. Checks on missing data, ranges of values and internal consistencies were undertaken, and errors compared with original data forms if possible. For uniformity, values were set to missing if they were greater or less than six standard deviations from the mean. This enabled obvious errors to be excluded, and although some measurements truly were exceptionally large or small, they were very rare, and the main objective was to obtain a representative sample of each population. The same iterative process was applied to the derived variables, where, if it was obvious which original variable caused the outlying value this was also set to missing. Otherwise all original variables used in the derivation of the new variables were set to missing. None of the maternal measurements were affected by these criteria, and the only paternal measurements that were excluded were two weights in Kasaji. Neonatal length, and to a lesser extent placental weight, head circumference, chest circumference and birthweight were excluded for some individuals in some datasets. However, the maximum number excluded from any dataset was 14 out of 2428 CR lengths in Beijing, and the greatest number excluded from the datasets combined was 29 out of 20916 CH lengths.

2.6.4 Analysis methods

Distributions of continuous variables were examined. All neonatal anthropometric variables were approximately normally distributed. Maternal weight, BMI, MUAC, AMA and skinfold measurements had skewed distributions in most of the datasets, as did paternal BMI. Gestational duration and maternal age were also skewed in some of the datasets.

For normally distributed data, means and standard deviations (SDs) were presented. T-tests and analysis of variance (ANOVA) were used to test differences in means, and Pearson correlations used to examine the relationship between two continuous variables. For skewed variables, non-parametric methods were used. Medians and inter-quartile ranges (IQRs) were presented, and Mann-Whitney and Kruskal-Wallis tests used to compare differences between two, and more than two groups respectively. Relationships between two continuous variables were analysed using Spearman correlations. However,

log transformations were used to obtain normal variables for use in regression. Frequencies of categorical variables were calculated. Chi-squared tests were used to assess the relationship between two categorical variables.

Neonatal, maternal and paternal phenotypes were characterised using 'star graphs', where the rays of the stars represented different anthropometric measurements. Other descriptive multivariate techniques were considered, such as Chernoff faces (Chernoff 1973) and Andrews plots (Andrews 1972), but these were deemed unsuitable. For Chernoff faces, different facial features are used to represent each anthropometric measurement, but these diagrams are difficult to interpret, as the choice of facial features is so subjective. Andrews plots represent the data using finite Fourier series, but can only be used for small numbers of observations. In addition to the star graphs which provided useful visual representations of the data, a more statistically rigorous technique was also required, and for this principal components analysis (PCA) was chosen. Alternatives included cluster analysis and factor analysis. Cluster analysis may have been useful to identify natural groupings within the observations, but the resulting variables would have been categorical rather than continuous as in PCA, so a lot of information would have been lost. Factor analysis results would have been expected to be similar to those from PCA, although as this is a parametric method, more assumptions would have been required, and analysis would have been more complex.

A number of different regression-based methods were used to look at relationships between mothers and babies, father and babies, and also babies/mothers and later blood pressure. Details of each method used are given in the relevant chapters, where data can be used to ensure clarity of explanations.

Data cleaning was undertaken in SPSS 10 for Windows, while Stata version 7.0 was used for most analysis. Matlab version 6.1 was also used where necessary.

3 Placental weighing study

3.1 Introduction

One of the neonatal outcomes of interest was placental weight, and the method of preparation of placentas for weighing was inconsistent across the datasets. In some, usually those based on routine obstetric records, no preparation was undertaken. In others the placentas were trimmed, removing the umbilical cord and/or membranes, as well as any blood clots. Table 3.1 shows the division of datasets according to how the placentas were prepared for weighing.

Table 3.1 Placental preparation according to dataset

Untrimmed	Trimmed (cord and membranes)
Southampton 3	Southampton 1
Southampton 4	Southampton 2
Preston	Mysore 2
Sheffield	Pune 1
Farnborough	Pune 2
Isle of Man	Kasaji, Congo
Aberdeen	
Helsinki	
Mysore 1	
Beijing	
Imesi, Nigeria	
Kingston 1	

In Kingston 2, the membranes but not the cord were removed. Placental weight was not recorded in Kandy (Sri Lanka) or any of the seven WHO datasets.

An adjustment factor was required to enable comparisons to be made across the datasets. Although there were fewer datasets in which placentas had been trimmed, these were the ones that were used extensively in analyses due to their detailed maternal anthropometric measurements. It was also the placental weight itself that was of interest, excluding the cord and membranes. Hence it was decided that all untrimmed placentas should be adjusted to trimmed weights. No previous study has quantified the contribution of the cord and the membranes to untrimmed placenta weight. Therefore a small study was undertaken to establish this.

3.2 Methods

The study was undertaken in the Princess Anne Maternity Hospital, Southampton. Entry was restricted to singleton liveborns with complete placentas. It was requested that the placentas of babies born between 6am and 6pm on weekdays during the period 27th March to 16th May 2000 were refrigerated, although it was not possible to obtain a consecutive sample due to the many other responsibilities of the hospital staff. The placentas were weighed on the day of delivery by one of three research nurses. Data collection stopped at 50 placentas as this gave 90% power at the 5% significance level to detect a 12% reduction in weight after trimming, with standard deviation 25%.

After removal of obvious clots, the weight of the untrimmed placenta, complete with umbilical cord and membranes, was measured on digital scales. The placenta was weighed again after cutting the cord flush with its insertion into the placenta. A third measurement was made after stripping the amnion to the cord and trimming the chorion close to the placental edge (Figures 3.1a to c).

Figure 3.1a Untrimmed placenta

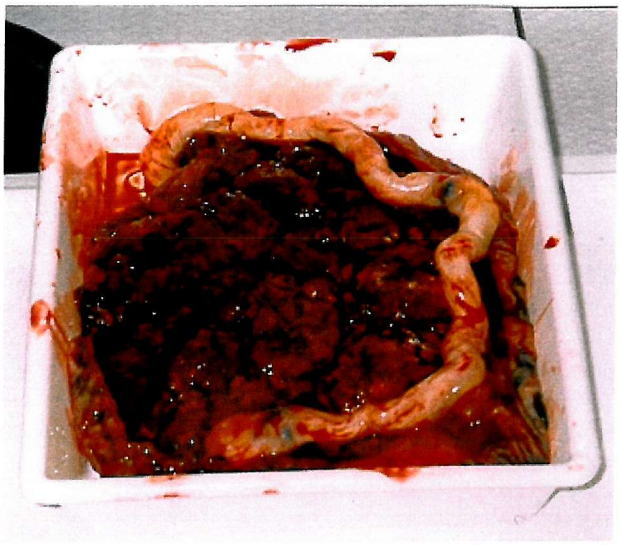


Figure 3.1b Trimming the umbilical cord

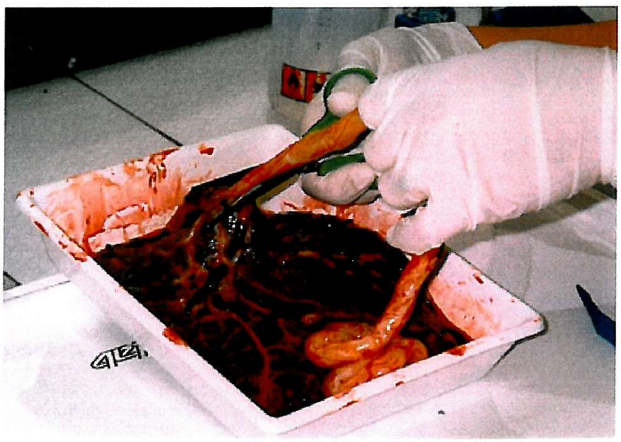
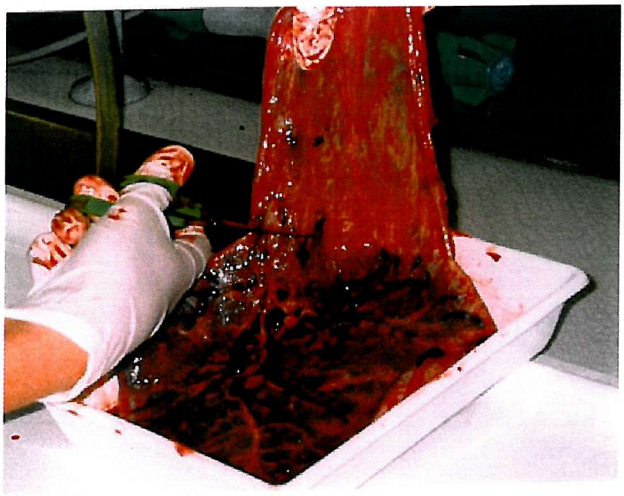


Figure 3.1c Trimming the membranes



The type of placental delivery (spontaneous expulsion, controlled cord traction or manual), time of placental weighing since delivery, and state of the membranes (complete, incomplete or doubtful) were also recorded.

In addition to placental data, the following information was also collected:

- mother's date of birth
- mother's diabetic status
- date and time of delivery
- type of labour (spontaneous, elective caesarean section, induced or augmented)
- duration of labour (each of the three stages in hours and minutes)
- method of delivery (normal vaginal, instrumental, elective caesarean section or emergency caesarean section)
- presentation at delivery (vertex/cephalic or breech)
- infant sex
- estimated gestational age in weeks and days
- birthweight in grams

The form used for data collection is in Appendix 1.

3.3 Results

3.3.1 Study sample

The mean age of the mothers at delivery was 32, and ranged from 20 to 44 years. None were diabetic, although one had impaired glucose tolerance.

48% had spontaneous labour, and of these, 92% had normal vaginal deliveries (NVD) and the rest had emergency caesarean section deliveries (CSD). 8% of women had labour induced. Half of these had NVD and the other half had emergency CSD. The remaining 44% had elective CSD. 12% of the babies were breech, and these were all elective CSD. In those that had a spontaneous labour and NVD, the median duration of labour was 3 hours 8 minutes for stage 1, 18 minutes for stage 2 and 7 minutes for stage 3. The median overall duration was 4 hours.

56% of the babies were male. The median (IQR) length of gestation was 39 (38, 40) weeks, and 6% were preterm. The median (IQR) birthweight for all babies was 3.6 (3.1, 3.8)kg.

3.3.2 Placental data

The median (IQR) time between delivery and placental weighing was 2 hours 20 minutes (1 hour 29 minutes, 4 hours 6 minutes). 90% of the placentas were delivered by controlled cord traction, 6% by spontaneous expulsion and 4% manually. In all except one, the membranes were complete. Table 3.2 shows the median and IQRs for the three placental weights.

Table 3.2 Median (IQR) placental weights

Placental weight	Median	IQR
Before trimming	588g	496, 688g
After cord removed	540g	471, 659g
After cord and membranes removed	480g	410, 580g

Spearman correlation coefficients with the trimmed weight were 0.98 for the untrimmed weight, 0.54 for the combined weight of the cord and the membranes, 0.36 for the cord weight and 0.54 for the membrane weight ($p<0.05$ for all).

As significant correlations were seen between the trimmed weight and the weight of the cord and membranes, percentages as opposed to absolute differences were used for analysis. The percentage differences were calculated as

$$\frac{\text{(untrimmed weight – trimmed weight)}}{\text{untrimmed weight}} \times 100$$

The median (IQR) difference between untrimmed and trimmed placentas was 16.3 (13.5, 19.4)%. 5.5 (4.0, 7.5)% could be attributed to the cord, and the remaining 10.0 (8.9, 12.1)% to the membranes. The median (IQR) ratio of membrane to cord weight was 1.9 (1.3, 2.4).

3.3.3 Predictors of differences in placental weight

Median values for the percentage difference between untrimmed and trimmed (cord and membranes) placental weight for the lower and upper quartile of each continuous variable are displayed in Table 3.3. P-values for univariate regression models with logged percentage difference in placental weight as the outcome are also given.

Table 3.3 Continuous predictors of percentage differences in placental weight

	Quartiles	Median	p-value
Maternal age	Lower (< 29 years)	16.3	0.5
	Upper (> 35 years)	14.9	
Labour duration*			
Stage 1	Lower (< 110 mins)	16.7	0.3
	Upper (> 300 mins)	18.8	
Stage 2	Lower (< 7 mins)	16.7	0.2
	Upper (> 59 mins)	18.8	
Stage 3	Lower (< 5 mins)	19.1	0.3
	Upper (> 9 mins)	22.2	
Total	Lower (<127 mins)	16.7	0.3
	Upper (> 370 mins)	20.9	
Birthweight	Lower (< 3125g)	15.3	0.2
	Upper (> 3835g)	17.3	
Gestation	Lower (< 267 days)	16.1	0.4
	Upper (> 281 days)	19.0	
Time before weighing	Lower (< 89 mins)	17.3	0.3
	Upper (>246 mins)	16.4	

* restricted to spontaneous labour with normal vaginal delivery

Table 3.4 shows the median values for the percentage difference between untrimmed and trimmed weight in each group for the categorical variables. The p-values were from a Kruskal Wallis test.

Table 3.4 Categorical predictors of percentage differences in placental weight

		N	Median	p-value
Type of labour	Spontaneous expulsion	24	18.1	
	Elective caesarean section	22	14.6	
	Induced	4	14.8	0.01
Mode of delivery	Normal vaginal delivery	24	19.0	
	Elective caesarean section	22	14.6	
	Emergency caesarean section	4	14.4	0.001
Presentation at delivery	Vertex/cephalic	44	16.7	
	Breech	6	13.4	0.049
Sex	Male	28	16.5	
	Female	22	16.2	0.6
Term baby	No	3	17.0	
	Yes	47	16.1	0.4
Placental delivery	Spontaneous	3	18.8	
	Controlled cord contraction	45	16.4	
	Manual	2	11.9	0.1
Measurer	1	18	16.7	
	2	26	16.3	
	3	6	15.8	0.9

The only significant predictors of the percentage difference between untrimmed and trimmed placental weight were the type of labour, mode of delivery and presentation at delivery. Both the type of labour and presentation at delivery were confounded by the mode of delivery. For example, if labour was spontaneous, the mode of delivery could not be elective CS. Hence the mode of delivery was the only variable requiring further investigation.

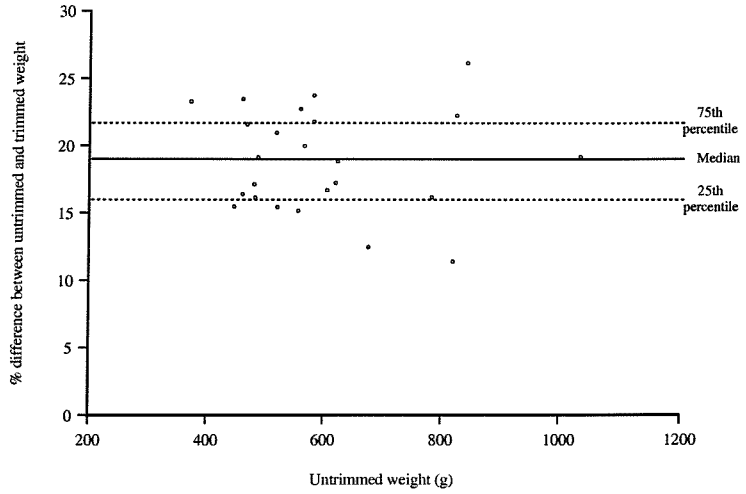
The median difference for the combined elective and emergency CSD groups was 14.4%, which was significantly lower than the median difference of 19.0% in the NVD group (p=0.001). The differences between these groups were more marked in the cord (7.0% NVD vs 4.5% CSD, p=0.001) than the membranes (10.7% NVD vs 9.4% CSD, p=0.04).

52% of the deliveries in this study were caesarean sections, which was not representative of all deliveries in the hospital (21%, September 2000). The proportion was higher than expected as this type of delivery was more likely to occur in the daytime, which was when the study took place. As the proportion was likely to be substantially larger than in the populations that required adjustment, the adjustment factor was calculated after exclusion of those who had CSD. The measured characteristics of the remaining 24 were not significantly different from those who had been excluded, except that their gestations were longer. Within the NVD group, none of the variables in Tables 3.3 and 3.4 had a

significant effect on the percentage difference in placental weight before and after trimming.

The median (IQR) percentage difference between untrimmed and trimmed placental weight for the NVD group was 19.0 (16.1, 22.1)%. Figure 3.2 shows the percentage difference in untrimmed and trimmed weight, according to the absolute untrimmed weight.

Figure 3.2 Percentage difference according to untrimmed weight



There was a slight increase in the variation of the percentage difference as the untrimmed weight increased. However, it seemed reasonable to use this adjustment across the whole range of untrimmed weights.

19% was subtracted from placentas in all datasets where trimming had not been undertaken before weighting (10.7% in Kingston 2 as placentas had been partially trimmed), and these values used throughout analysis.

3.4 Summary

- The mode of delivery was the only factor that affected the percentage difference in untrimmed and trimmed placental weight.
- Excluding caesarean section deliveries, the difference between untrimmed and trimmed placental weight was 19%.

The findings described in this chapter have been published (Leary et al. 2003).

4 Characterisation of neonatal phenotypes

The geographical differences in neonatal phenotypes between and within countries were characterised using the 20 datasets in the main study (§4.1). Selected analyses were then repeated using the seven WHO datasets in addition to the main study datasets (§4.2). As the WHO datasets were obtained from a common protocol, this would enable conclusions to be made with more confidence. However, the inclusion criterion for the WHO datasets stated that all neonates had to weigh at least 2500g at birth and their mothers had to have previously breastfed. Hence all datasets in the main study were also restricted to multips weighing at least 2500g at birth for these analyses. The adequacy of various indices of adiposity was also investigated using all datasets without restrictions (§4.3).

In a few of the datasets there were some non-random missing values. In Sheffield abdominal circumference was only recorded after 1922, so measurements were missing for over a third of the neonates. Placental weight was only recorded after 1975 in Mysore 1, so over a third were missing. Birthweight was the only measurement recorded in Kandy (Sri Lanka) for the last three months of the study. Therefore just over two fifths of length and head values were not randomly missing. In Kasaji (Congo), chest circumference was only measured from 1997, so just under half of the values were missing.

In each of these datasets, there were no significant differences in birthweight between those that had other anthropometric measurements recorded and those that did not. However, those with data recorded for abdominal circumference in Sheffield, placental weight in Mysore 1 and chest circumference in Kasaji tended to be shorter and have smaller heads compared to those with missing data. Sex distributions were similar whether or not data were missing, and gestational duration did not differ by more than two days.

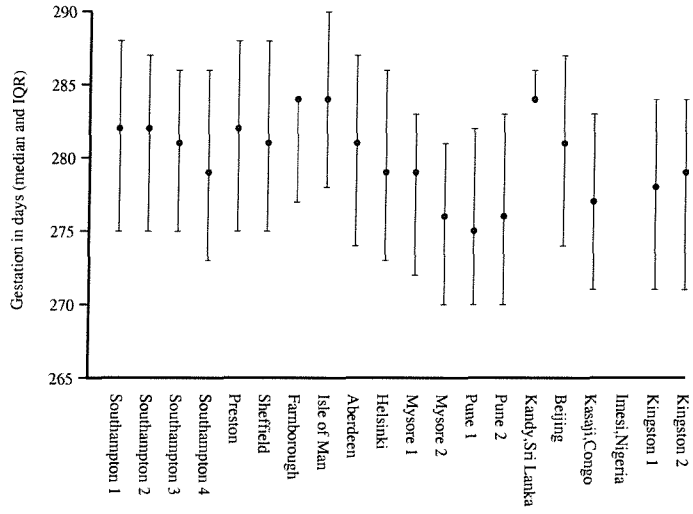
4.1 Main study analysis

4.1.1 Characteristics of datasets

Gestational duration

All neonates selected for analysis were between 259 and 308 days (37 and 44 weeks) gestation. In Imesi (Nigeria) exact gestations were not recorded, although all babies included were born at term as identified by the midwives. Figure 4.1 shows the median gestation with inter-quartile range (IQR) for each dataset.

Figure 4.1 Gestational duration according to dataset

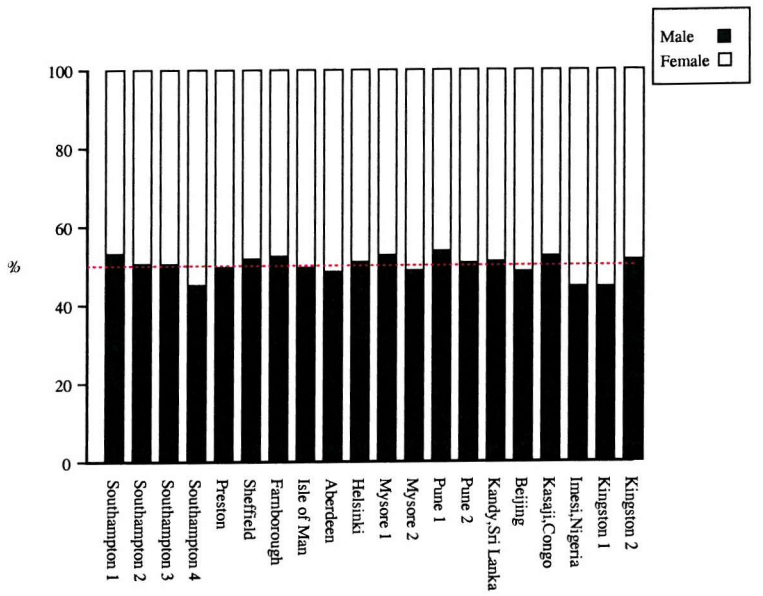


Durations were generally shorter in India and Africa and longer in the UK. The IQRs were similar with the exception of Farnborough where the median and 75th percentile were equal, and in Kandy where the median and 25th percentile were equal. This may be because these datasets originally recorded gestation in weeks rather than days.

Sex

Neonatal sex was present for all neonates in all datasets. Figure 4.2 shows that the proportion of males and females was similar across the datasets. The red dotted line indicates equal proportions of males and females.

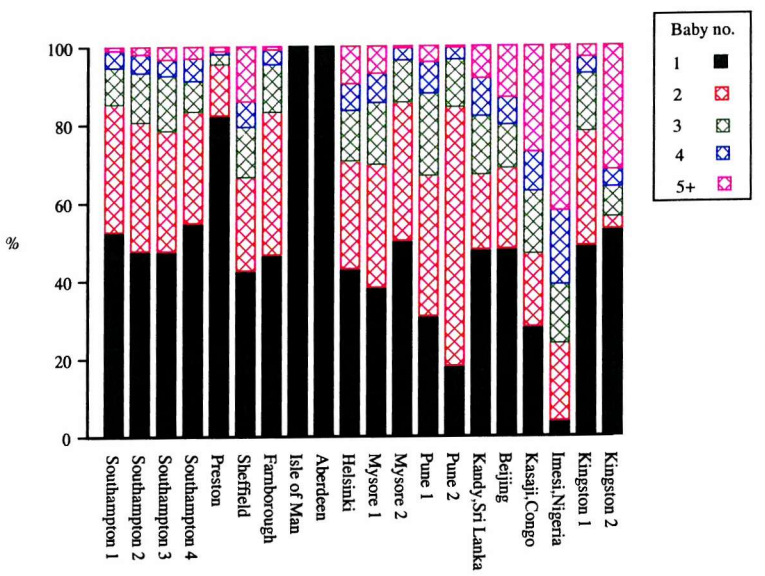
Figure 4.2 Sex distribution according to dataset



Parity

Parity was available in all datasets, although values were not recorded for some individuals. All neonates in Aberdeen and the Isle of Man were first born as required by entry criteria. Figure 4.3 shows parity split into five categories according to dataset.

Figure 4.3 Parity distribution according to dataset

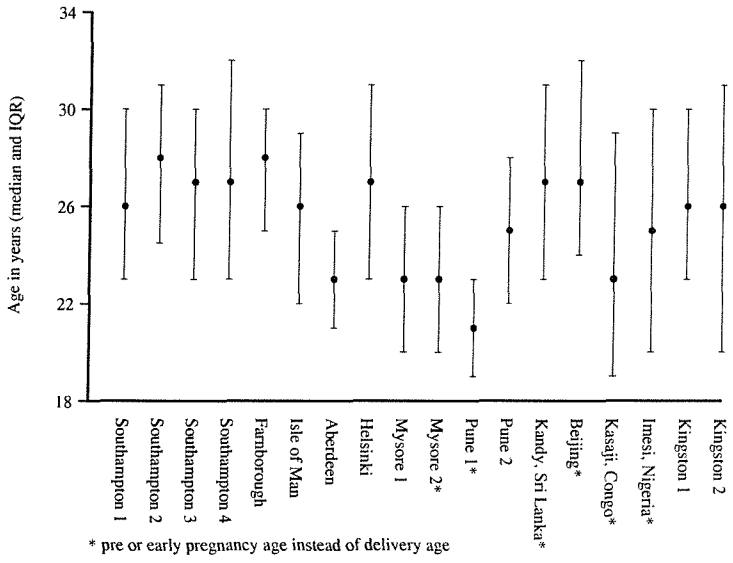


The lowest proportion of first borns was in Imesi. The highest proportion was in Preston, and the parity distribution in this dataset was unexpectedly different from Sheffield, which was a similar study. In all datasets with multiparity, there were some neonates who were the fifth child or higher within their family. This proportion was highest in Imesi and lowest in Mysore 2 and Pune 2.

Maternal age

Maternal age was available in all datasets. Age at delivery was used if it had been recorded, otherwise age at an earlier timepoint or before pregnancy was used (Figure 4.4). For a small number of mothers age had not been recorded at any timepoint.

Figure 4.4 Maternal age distribution, according to dataset



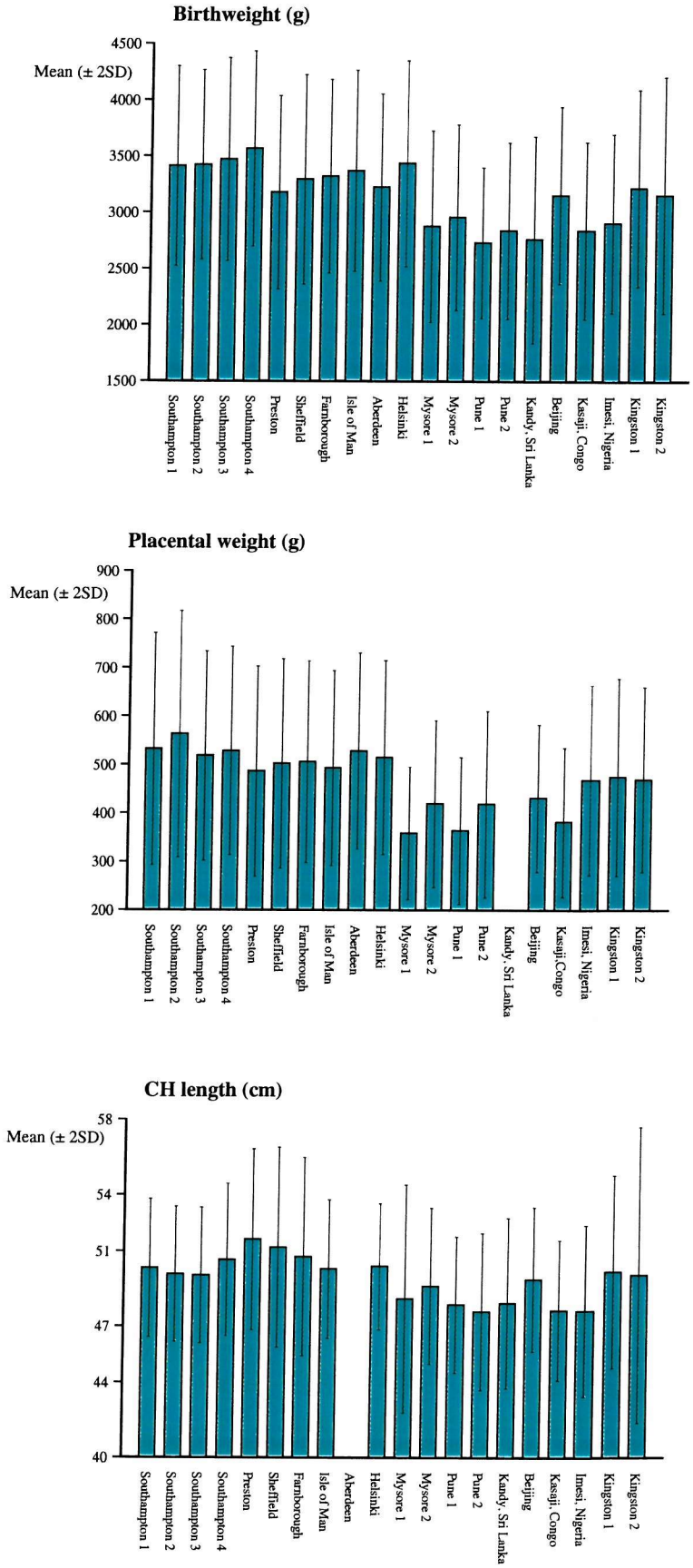
Mothers were generally younger in India and Africa, and older in Southampton. IQRs tended to be wider in places with older mothers.

4.1.2 Size of neonates

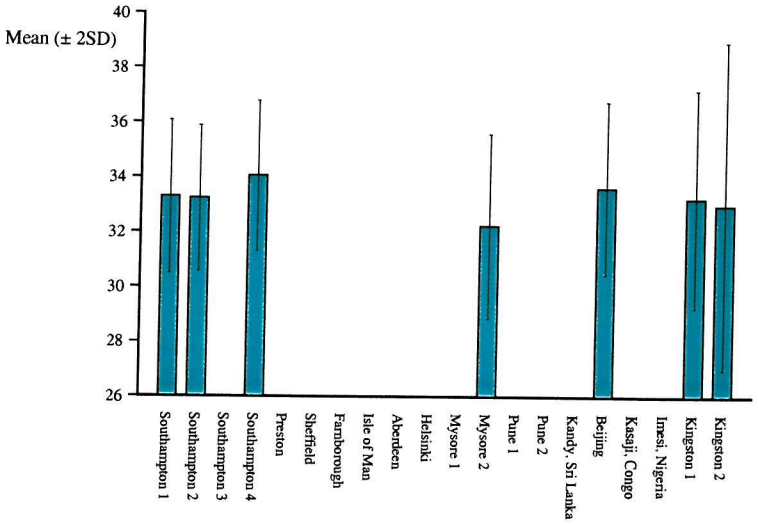
Mean measurements

Figure 4.5 shows the mean values with standard deviations (SDs) for the neonatal measurements available in each dataset. Values were adjusted to 40 weeks gestation (males and females separately) using regression for all datasets except Imesi. All measurements were approximately normally distributed. Tables of mean values can be found in Appendix 2a.

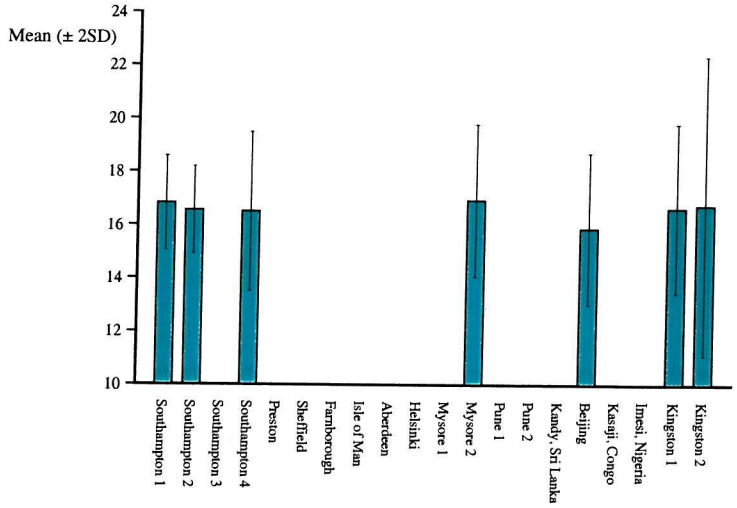
Figure 4.5 Mean (SD) measurements



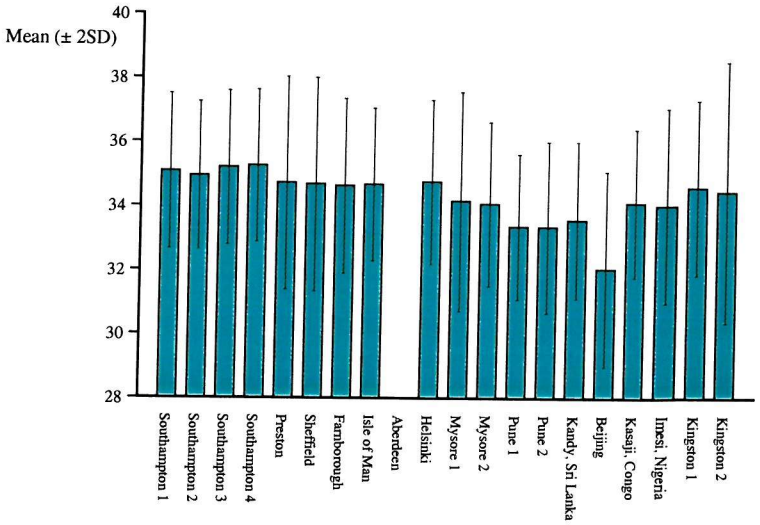
CR length (cm)



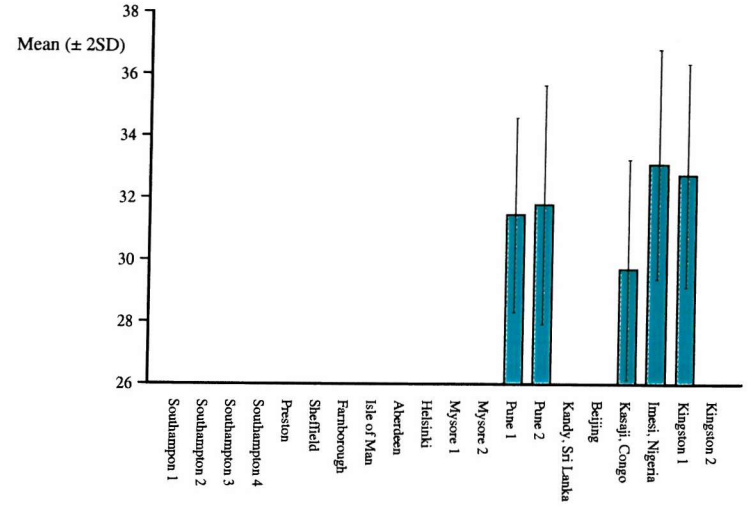
Leg length (cm)



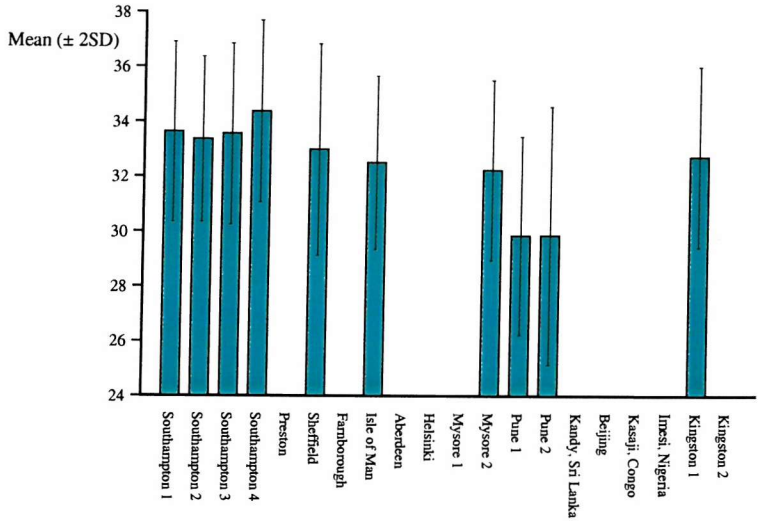
Head circumference (cm)



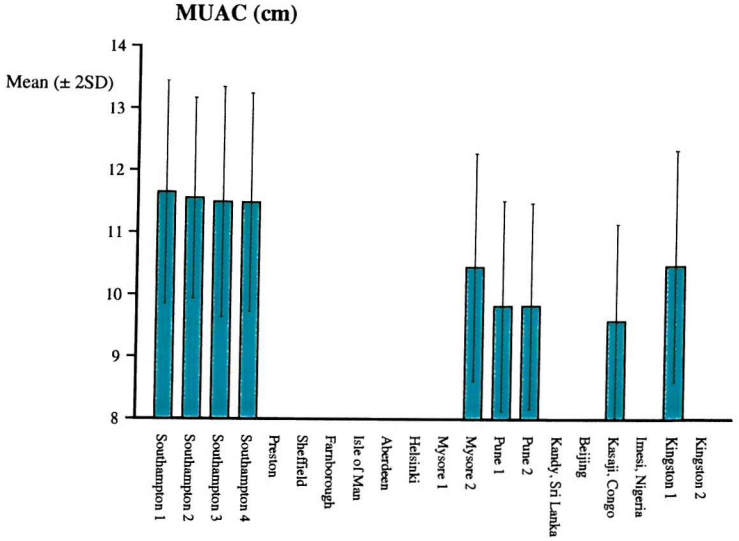
Chest circumference (cm)

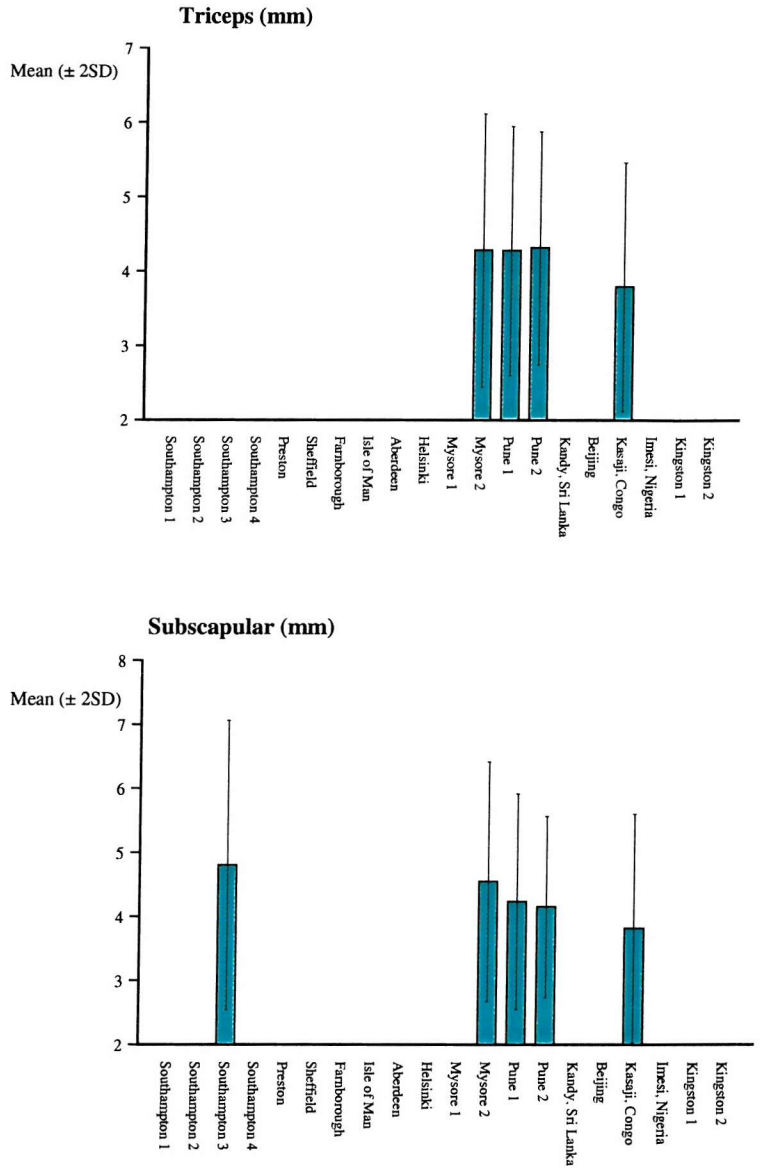


Abdominal circumference (cm)



MUAC (cm)





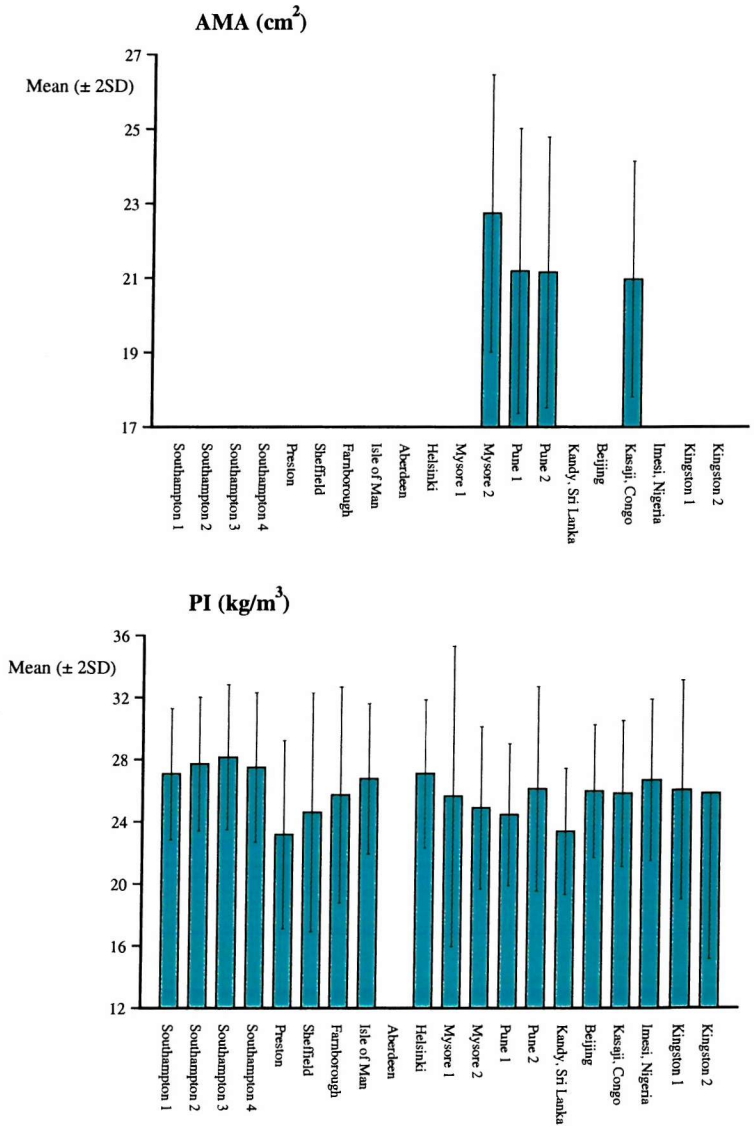
European neonates were generally the largest in all dimensions, followed by the Jamaicans, Chinese then Indians, Sri Lankans and Africans. The lowest birthweights, placental weights and abdominal circumferences (measured at the xiphisternum) were seen in Pune 1, the only rural Indian population. Africans were the shortest, and the neonates in Kasaji had much smaller chest circumferences (measured at the nipple), MUACs and skinfolds. The Chinese had substantially smaller head circumferences. They also had short legs but long bodies, while those from Mysore 2 had short bodies but long legs. The Indian neonates had reduced mid-upper-arm circumferences (MUAC) compared to the European populations, but their subscapular skinfolds were similar.

Within the European populations, the Southampton neonates tended to be the largest, which may be due to secular trends as these neonates were born most recently. However,

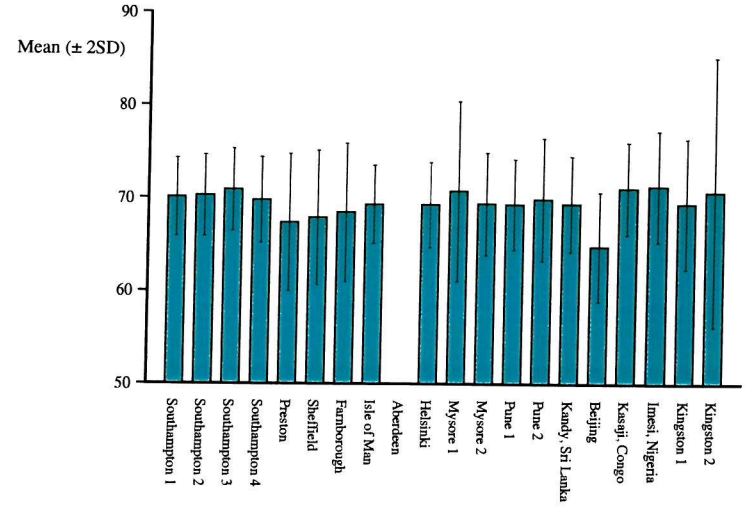
crown-heel (CH) lengths were larger in the earlier datasets, in particular Preston and Sheffield. This is likely to reflect measurement error, as data were taken from obstetric records for these populations, and length is a difficult measurement to make without special equipment. Within the Indian populations, the neonates from Pune 1, the only rural population tended to have the smallest measurements, while the largest were seen in Mysore 2. Sri Lankan neonates were similar to the rural Indians, although slightly larger in all measurements. Nigerian neonates had higher birthweights and much higher placental weights and chest circumferences than those from Kasaji, although CH lengths and head circumferences were similar in these two populations.

Arm muscle area (AMA) was calculated using MUAC and triceps skinfold. Ratios of the direct measurements were also calculated as percentages to compare the shapes of neonates in the different populations. Mean values with SDs for these derived variables are shown in Figure 4.6.

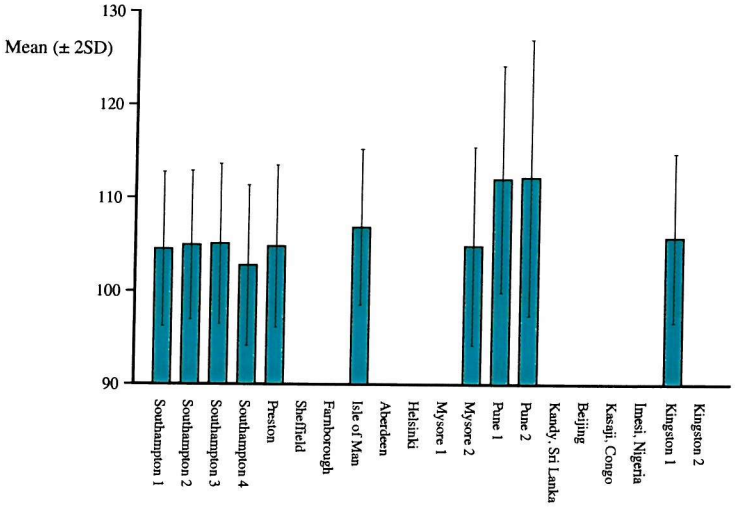
Figure 4.6 Mean (SD) derived measurements



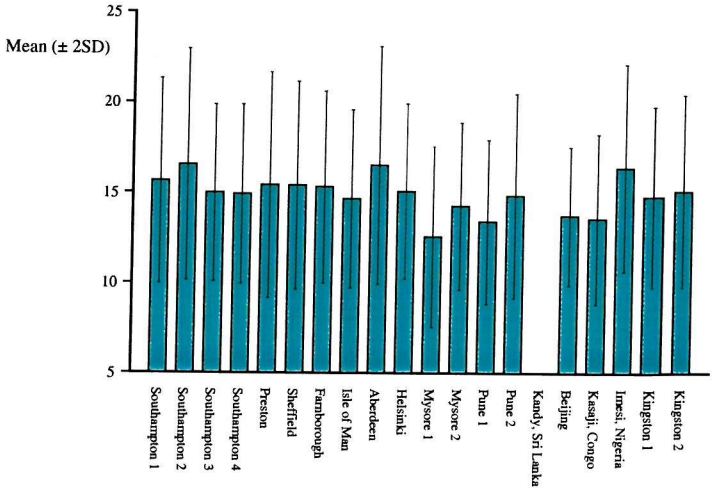
Head to length ratio



Head to abdomen ratio



Placenta to birthweight ratio



Patterns for AMA were similar to those for MUAC. Neonates from Pune and particularly Kasaji had reduced AMA compared to Mysore 2. European neonates were fattest according to ponderal index (PI), with the exception of those in Sheffield, Preston and Farnborough who were thin, due to long lengths. African, Chinese and Jamaican neonates were all relatively 'fat'. Of particular importance is the observation that neonates from Kasaji had an average PI in relation to the other datasets despite being substantially smaller for many of the direct measurements. The Indians were thinner, and the Sri Lankan neonates were the thinnest of all.

The head to abdomen and head to length ratios are traditionally used to indicate the extent of sustained brain growth at the expense of other development. Both ratios were calculated as abdominal circumference was only recorded in a few of the datasets. African and Indian neonates had large heads in relation to their other dimensions, while the Chinese had small relative head growth. Although the placenta to birthweight ratios were similar in the different populations, the highest values were seen in Imesi, suggesting less efficiency of the placenta, and the lowest in India, China and Kasaji.

Coefficients of variation (CVs) were used to compare the mean values across the datasets for each neonatal measurement. These were derived using the following formulae:

$$CV = [\, SD\,(\bar{x}_i) / \bar{X}\,] \times 100$$

where $\bar{x}$ = mean for dataset i, i = 1 - 20 $\quad\quad$ $\bar{X}$ = overall mean.

Results are shown in Table 4.1, where variables are shown in descending order of CVs to aid interpretation.

Table 4.1 Coefficients of variation for each measurement

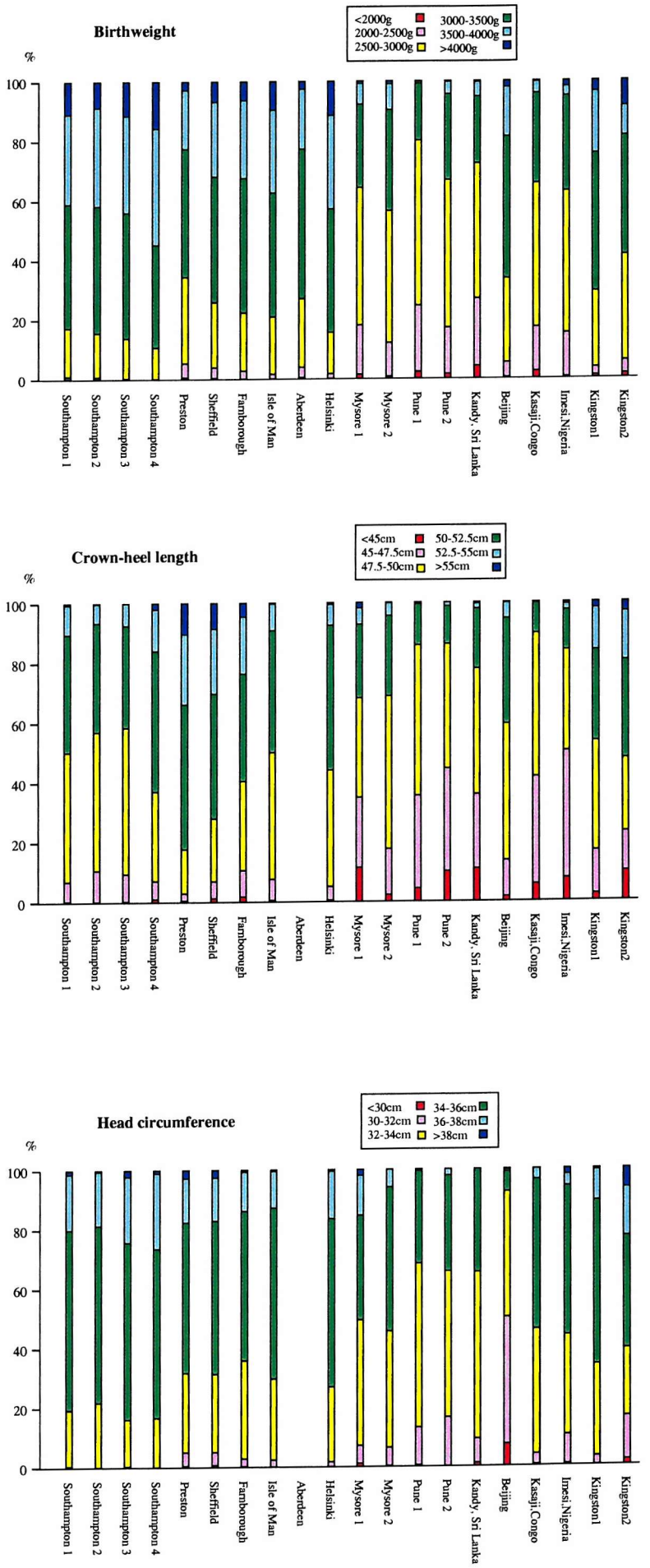
Measurement	CV	SD (dataset means)	Overall mean
Placental weight (g)	12.6%	61	485
Subscapular (mm)	8.7%	0.4	4.3
Birthweight (g)	8.1%	262	3247
MUAC (cm)	7.9%	0.8	10.7
Placenta to birthweight ratio (%)	7.4%	1.1	14.9
Triceps (mm)	6.0%	0.3	4.2
PI (kg/m^3)	5.3%	1.4	25.9
Abdomen (cm)	4.7%	1.5	32.6
Chest (cm)	4.2%	1.3	31.9
AMA (cm^2)	3.8%	0.8	21.7
Head to abdomen ratio (%)	3.0%	3.2	105.9
Head (cm)	2.3%	0.8	34.3
CH length (cm)	2.3%	1.2	50.1
Head to length ratio (%)	2.2%	1.5	68.5
Leg (cm)	2.1%	0.3	16.3
CR length (cm)	1.7%	0.6	33.3

There was generally wide variation in the measurements between populations, particularly placental weight and birthweight. There was relatively less variation in crown-rump (CR) length and leg length. The CV for head circumference decreased to 1.7% if Beijing was excluded, indicating that this measurement was relatively similar in all populations, although markedly reduced in Beijing.

Grouped measurements

Birthweight, CH length and head circumference, all adjusted for gestation, were each divided into six groups. The proportions within each group were plotted for all datasets, as seen in Figure 4.7.

Figure 4.7 Grouped measurements according to dataset



None of the neonates in Europe and Beijing weighed less than 2000g, while none in Pune, Kandy and Kasaji weighed more than 4000g at birth. The largest proportion of neonates weighed 2500 to 3000g in India, Sri Lanka and Africa. This increased to 3000 to 3500g in Europe, China and Jamaica.

In general, patterns for CH length and head size were similar to those seen for birthweight. However, Beijing had the highest proportion of neonates with heads less than 30cm compared to other datasets. It was also the only dataset where the largest proportion of neonates had heads that were between 30 and 32cms.

4.1.3 Shape of neonates

Multivariate techniques were implemented to investigate geographical variation in the shape of neonates. All datasets except Aberdeen contained measurements of birthweight, CH length and head circumference. Analyses were based on mean values of these variables for each dataset, adjusted for gestation.

Star graphs

Internally derived star diagrams were constructed such that the lengths of the rays of the stars were proportional to the relative magnitudes of the birth measurements (Siegal et al. 1971), as measurements were made in different units so absolute values could not be used. To prevent the smallest measurements for each variable being given rays of length zero, a 'smallest baby' was constructed using the minimum value minus SD for each measurement. These values were derived from the dataset of means from each population and are shown in Table 4.2.

Table 4.2 Values used for star graph 'smallest baby'

Variable	Minimum (of dataset means)	SD (of dataset means)	Minimum - SD
Birthweight (g)	2731.333	261.753	2469.580
CH length (cm)	47.784	1.169	46.615
Head circumference (cm)	32.027	0.792	31.235

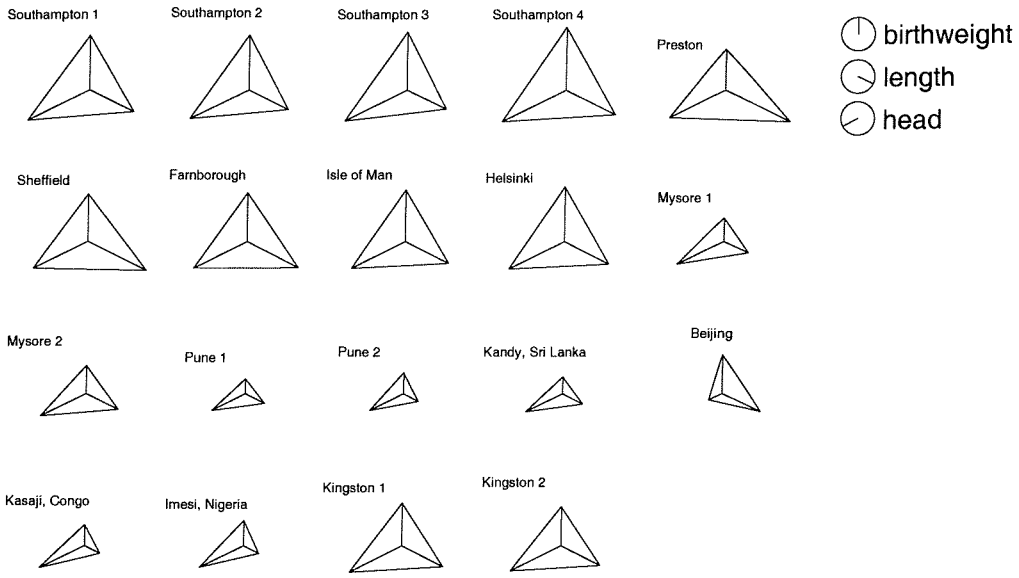
The ray for the largest value for each measurement, based on the datasets means, was given length one unit. Ray lengths for each measurement in all other datasets were calculated using the following formula:

$$\frac{\text{(dataset value- minimum value)}}{\text{(maximum value – minimum value)}}$$

where the largest of all the dataset means was used as the maximum, and the 'smallest baby' value was used as the minimum.

In Figure 4.8, the vertical ray represents birthweight, the ray pointing to the bottom right represents CH length, and the ray pointing down to the left represents head circumference.

Figure 4.8 Star graphs using birthweight, length and head circumference



European neonates were the largest and of a similar size. Jamaicans were slightly smaller, followed by substantially smaller neonates in China, Africa, India and Sri Lanka. Although all measurements varied across the populations, the main differences were in the ratio of head to length. Relative to length, neonates had larger heads in India, Sri Lanka and Africa, and to a lesser extent Europe except in Sheffield and Preston where they were particularly long. Neonates in China had very small heads in relation to length.

Principal components analysis

The above analysis provided a useful visual representations of the geographical differences in neonates. However, as interpretation of these star graphs is subjective, it was also necessary to use a more statistically rigorous technique, namely principal components analysis (PCA) (Hotelling 1933). This involves transforming an original set

of correlated variables to a new set of uncorrelated variables known as principal components (PCs). These PCs are linear combinations of the original variables. They are derived in decreasing order of importance such that the first PC accounts for as much of the variation in the original data as possible, and aiming for the first few components to contain nearly all the variation. This method is scale-dependent, and hence the derived PC's will vary according to the units used to measure the original variables. In addition, if some variables have a much greater range of values, they will dominate the first few PCs. To overcome this PCA can be performed on standardised variables (zero mean and unit variance). This is equivalent to deriving PCs from the correlation rather than the covariance matrix.

PCA can be performed on mean values from each dataset or on pooled individual values, and for these datasets, results were similar using either approach. However it was preferable to use means, due to the large variation in numbers in the datasets. Using individual values would have resulted in the larger datasets having more influence on the derivation of principal components than the smaller studies. The main objectives of PCA are to reduce dimensionality to enable graphical representation of the data, and to attempt to identify meaningful underlying new variables.

The first PC accounted for 79%, and the first two PCs for 94% of the variation in the data. These two PCs are presented in Table 4.3. Hence the first PC is equal to
0.61 × birthweight + 0.58 × CH length + 0.54 × head (all variables standardised).

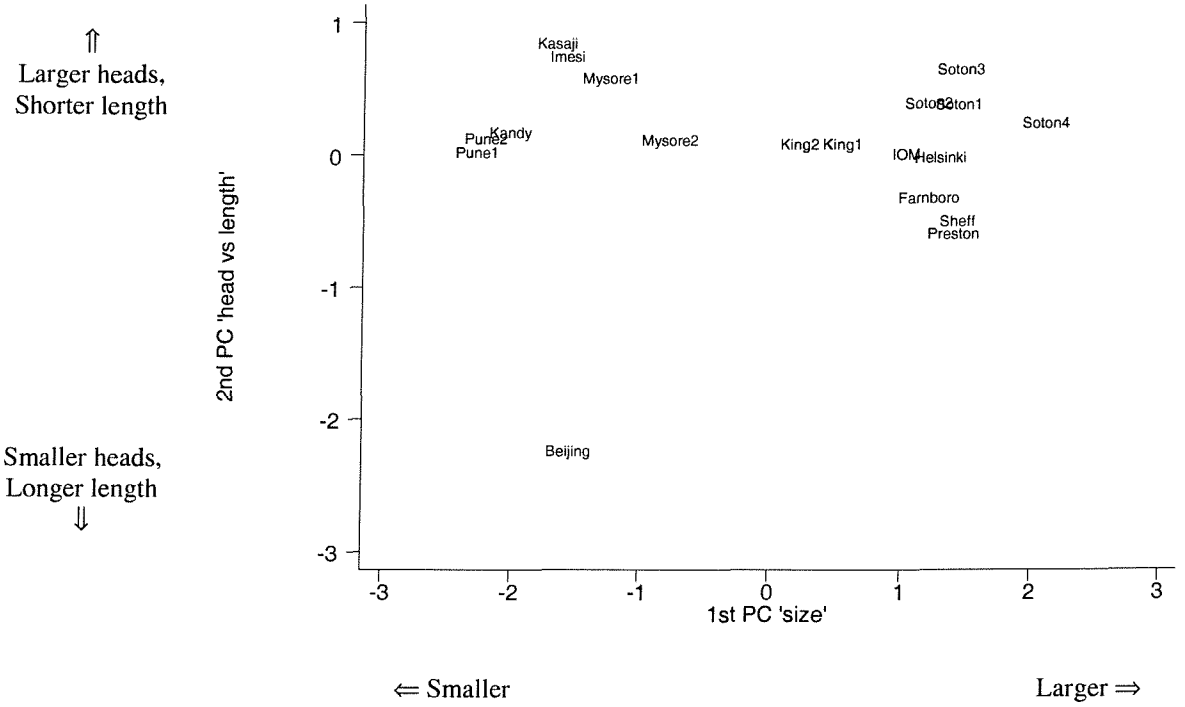
Table 4.3 Principal components using birthweight, length and head circumference

Original variable	PC1	PC2
Birthweight	0.61	-0.17
CH length	0.58	-0.57
Head circumference	0.54	0.80

As the coefficients of the first PC were all positive and of a similar size, this component reflected the overall size of the neonate. In the second PC, the coefficients for length and head circumference were of a similar size although had opposite signs, while the coefficient for birthweight was relatively small. This could be interpreted as a contrast between length and head size. Neonates with higher values on this PC had large heads relative to their lengths.

A scatter plot of the first two PCs could be used to identify clusters in the data (Figure 4.9).

Figure 4.9 Principal components using birthweight, length and head circumference



The European and Jamaican neonates were the largest, with similar relative proportions of head to length. The other neonates were much smaller. The Indians, Sri Lankans and particularly Africans had large heads relative to their lengths, while the Chinese had very small heads relative to their lengths. Results were similar after excluding Beijing, although birthweight became more important, acting in the same direction as CH length.

Further analysis was limited, due to different measurements being recorded in different datasets. However, placental weight was available in all except Kandy, and when this measure was added to analysis with birthweight, CH length and head, the first PC was a weighted average of all the variables, while the second was still a contrast between head and length, as the coefficient for placental weight was relatively small and the other coefficients remained similar. Hence, knowledge of placental weight did not aid distinction between neonates in different populations to a great extent. Alternatively, subscapular and MUAC could be added to birthweight, CH length and head, and this PCA yielded a second component that was a contrast between skeleton and fat. However, these results must be interpreted with caution as they were based only on one Southampton, three Indian and one African dataset. Additional PCA results are shown in Appendix 2b.

4.1.4 Intercorrelations between measurements

Pearson correlation coefficients between each pair of neonatal measurements, based on individual values and adjusted for gestation are shown in Appendix 2c. Colours are used to indicate the size of the correlation.

In each dataset, most of the direct measures (i.e. all measures except ratios) were positively correlated, such that babies that were larger in one measurement tended to also be larger in other measurements. Correlations were particularly strong between birthweight and chest, abdomen, MUAC and AMA, and also within the latter four measurements. CH length was consistently highly correlated with both CR and leg length, as were the triceps and subscapular skinfolds with each other. However, relationships with leg length were inconsistent across the datasets for some of the measurements. In the Southampton datasets, leg length was positively correlated with all available measurements. In Mysore 2, Beijing and Kingston, leg length was either weakly negatively correlated or not correlated with CR length. Also in Mysore 2, there were no correlations between leg length and head circumference or any measures of muscle and fat.

PI was positively correlated with all the direct measurements except length in most of the datasets. This index was negatively correlated with leg length, and also CH length in most datasets. However, inconsistent relationships were seen with CR length across the datasets. In Southampton, PI and CR length were not related, while in Mysore 2 and Beijing there were weak positive correlations, and in Kingston there were stronger negative correlations. The head to abdomen ratio was negatively correlated with the direct measurements in most datasets, particularly the abdominal circumference. The placenta to birthweight ratio was strongly positively related to placental weight in each dataset, although there were no other correlations. Relationships with the head to length ratio were generally inconsistent across the datasets, although it was positively related to head circumference and negatively related to CH length. PI was positively related to the head to length ratio, and negatively related to the head to abdomen ratio in all datasets. There were generally no relationships between PI and the placenta to birthweight ratio.

Although there were some variations in the correlation coefficients when the sexes were considered separately, the overall patterns remained the same.

4.1.5 Sex differences in size and shape

Mean gestation adjusted measurements for males and females in each dataset are shown in Appendix 2d. P-values to assess the significance of any differences (derived from t-tests) are also given.

Males were heavier and longer (CH, CR and leg length) than females, with larger head, chest and abdominal circumferences and heavier placentas. They also had higher head to abdomen and slightly higher head to length ratios. MUAC and AMA values were generally larger for males, although were significantly larger for females in Kasaji. Females had bigger skinfolds and higher placenta to birthweight ratios than males. There were inconsistencies in the sex differences in PI across the datasets. Males had significantly higher PIs in Helsinki, while females had PIs that were significantly or borderline significantly higher in Southampton 1 and 2, Kandy, Beijing and Kasaji.

Star graphs were constructed for males and females separately, using birthweight, CH length and head circumference, and are shown in Figure 4.10. The same 'smallest baby' as §4.1.3 was used.

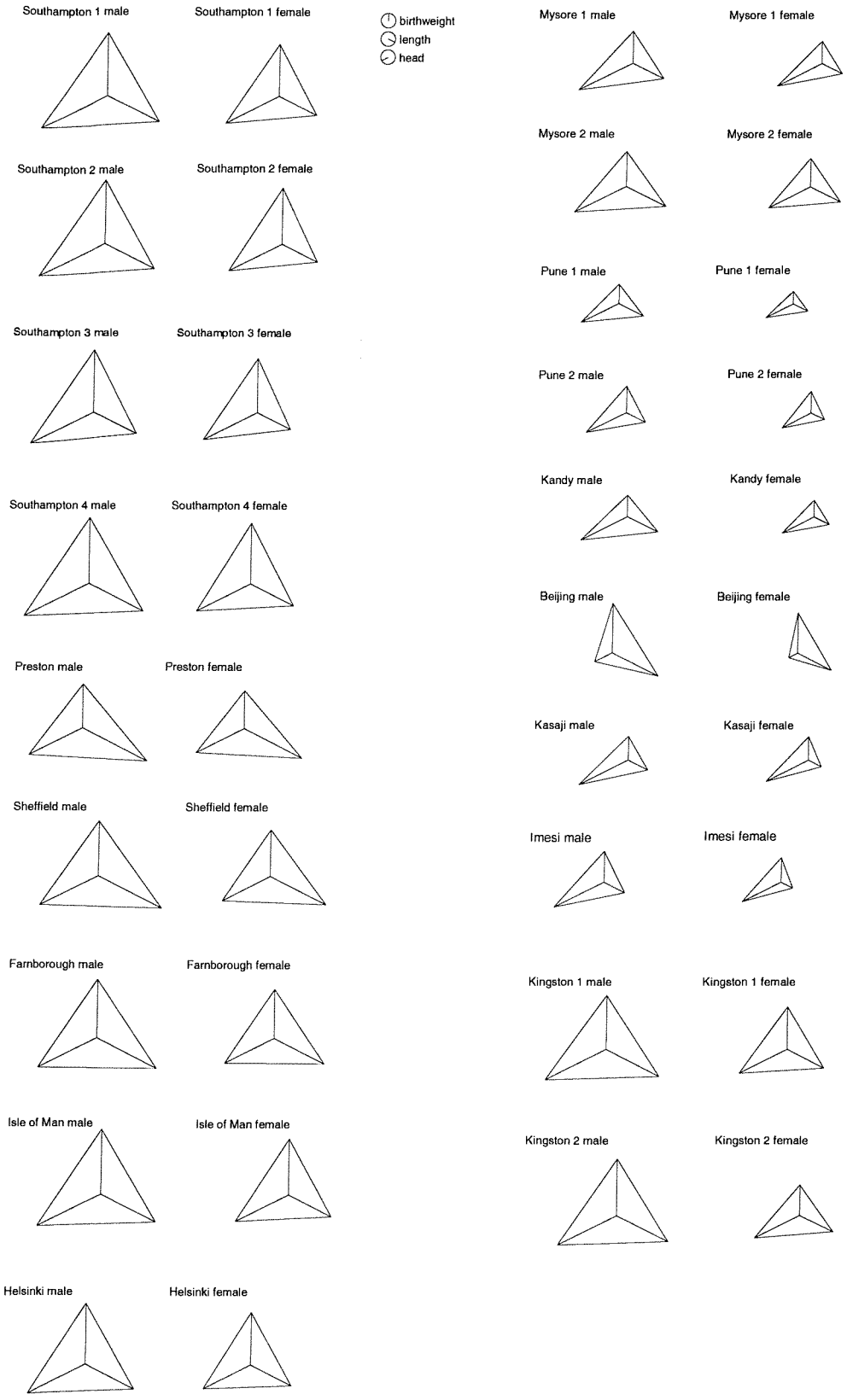
The differences in length of the rays of the star graphs between sexes are shown in Appendix 2e. These were calculated using the following formula for each dataset:

$$\frac{\text{(male value – female value)}}{\text{(maximum value – minimum value)}}$$

where the largest of all the dataset means for males and females separately was used as the maximum, and the 'smallest baby' value was used as the minimum.

Females were smaller than males in all datasets. They were of a similar shape, although in most datasets birthweight was the least reduced, followed by head circumference then CH length.

Figure 4.10 Star graphs for sex differences



4.1.6 Parity differences in size and shape

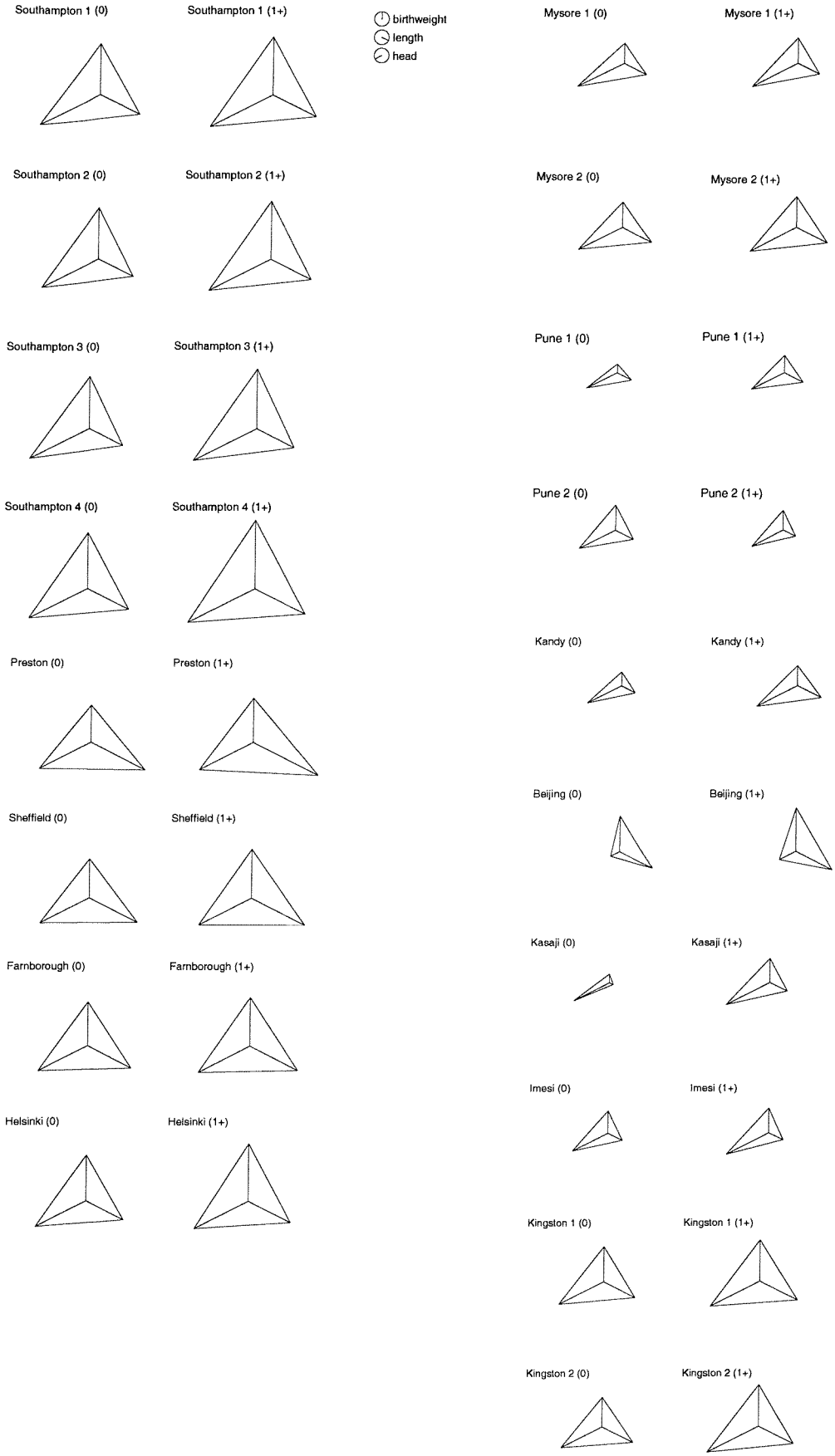
Parity was divided into two groups: zero and one or more. Mean gestation adjusted measurements for the groups in each dataset are shown in Appendix 2f. P-values to assess the significance of any differences (derived from t-tests) are also given.

First born neonates were lighter and shorter, with smaller head, chest, abdominal and mid-upper arm circumferences, AMA and lighter placentas. They also had smaller skinfolds and lower PIs. They had higher head to abdomen ratios. The parity differences in the ratios of head to length and also placenta to birthweight were inconsistent across the datasets. The head to length ratio was significantly higher for firstborns in Preston and Helsinki, but lower in Beijing and Kingston 2. The placenta to birthweight ratio was significantly or borderline significantly higher for firstborns in Helsinki, Kasaji and Imesi, but lower in Southampton 2 and Mysore 2. Patterns in Pune 2 were different from the above. First borns were larger in all measurements, although not significantly so.

Star graphs were constructed for the two parity groups using birthweight, CH length and head circumference, and are shown in Figure 4.11. Again, the same 'smallest baby' as §4.1.3 was used. Appendix 2g shows the differences in length of the rays of the star graphs between the two parity groups.

Firstborns were smaller than subsequent births in most datasets. They were of a similar shape, although head and length were generally less reduced than birthweight. Differences were more marked in the non-European countries.

Figure 4.11 Star graphs for parity differences



4.1.7 Maternal age differences in size and shape

Maternal age was divided into three groups: <20 years, 20-30 years and >30 years. Mean gestation adjusted measurements for the groups in each dataset are shown in Appendix 2h. P-values to assess the significance of any differences derived from ANOVAS are also given.

In general as maternal age increased, neonates were heavier with larger placentas. They were also longer, with greater head, chest, abdominal and mid-upper arm circumferences, more AMA, larger skinfolds and higher PIs. Older mothers tended to have neonates with higher head to length ratios, but lower head to abdomen and placenta to birthweight ratios. Relationships were stronger in the non-European countries.

Star graphs were constructed for the three maternal age groups using birthweight, CH length and head circumference, and are shown in Figure 4.12. The same 'smallest baby' as §4.1.3 was used. The differences in length of the rays of the star graphs between maternal age groups are shown in Appendix 2i.

Figure 4.12 Star graphs for maternal age differences

Older mothers had larger neonates, and these differences were much more distinct in the non-European countries. Neonates were of a similar shape, independent of their mother's age. However, in many of the datasets, head size and length were less reduced than birthweight.

4.2 Main and WHO study analysis

The size and shape analyses from §4.1 were repeated, using the 20 datasets in the main study restricted to multips (second born or higher) weighing at least 2500g at birth, and the seven datasets from the WHO study. It was not possible to include datasets from the Isle of Man and Aberdeen as in these, all neonates were first born. Table 4.4 shows the numbers of neonates within each dataset that were used.

Table 4.4 Numbers used for analysis – main and WHO study

Dataset	Number	% of original dataset excluded
Southampton 1	261	53.1%
Southampton 2	269	48.4%
Southampton 3	197	47.7%
Southampton 4	46	54.9%
Preston	172	83.0%
Sheffield	2550	42.3%
Farnborough	867	48.3%
Helsinki	3378	44.6%
Mysore 1	655	47.0%
Mysore 2	258	56.8%
Pune 1	330	47.9%
Pune 2	167	37.9%
Kandy, Sri Lanka	203	55.4%
Beijing	1213	50.1%
Kasaji, Congo	204	39.6%
Imesi, Nigeria	188	30.1%
Kingston 1	238	51.4%
Kingston 2	31	55.7%
WHO Sweden	505	N/A
WHO Australia	622	N/A
WHO Chile	688	N/A
WHO Guatemala	294	N/A
WHO India	504	N/A
WHO China	541	N/A
WHO Nigeria	512	N/A

4.2.1 Characteristics of datasets

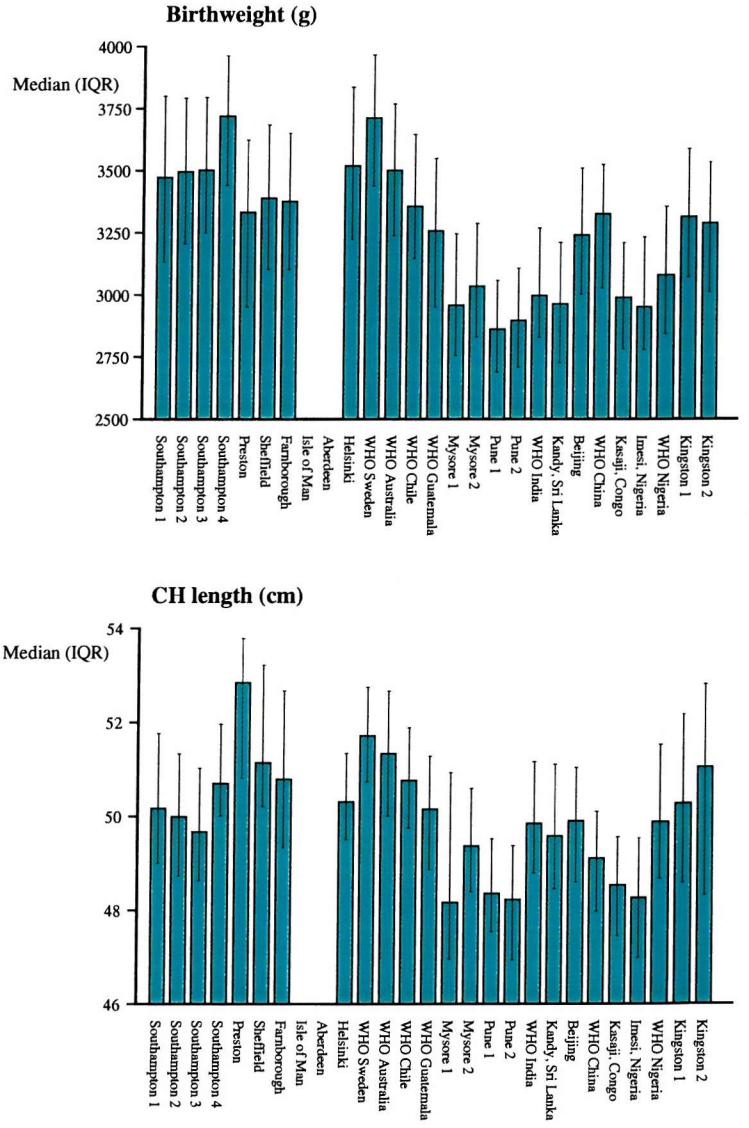
The median gestational duration was 39 weeks in Chile and India, and 40 weeks in the other WHO datasets. IQRs were all two weeks or less. These gestations were based on LMPs but had only been recorded in weeks. There was a slightly higher proportion of males than females in each of the WHO datasets. This ranged from 50.4% in Chile to

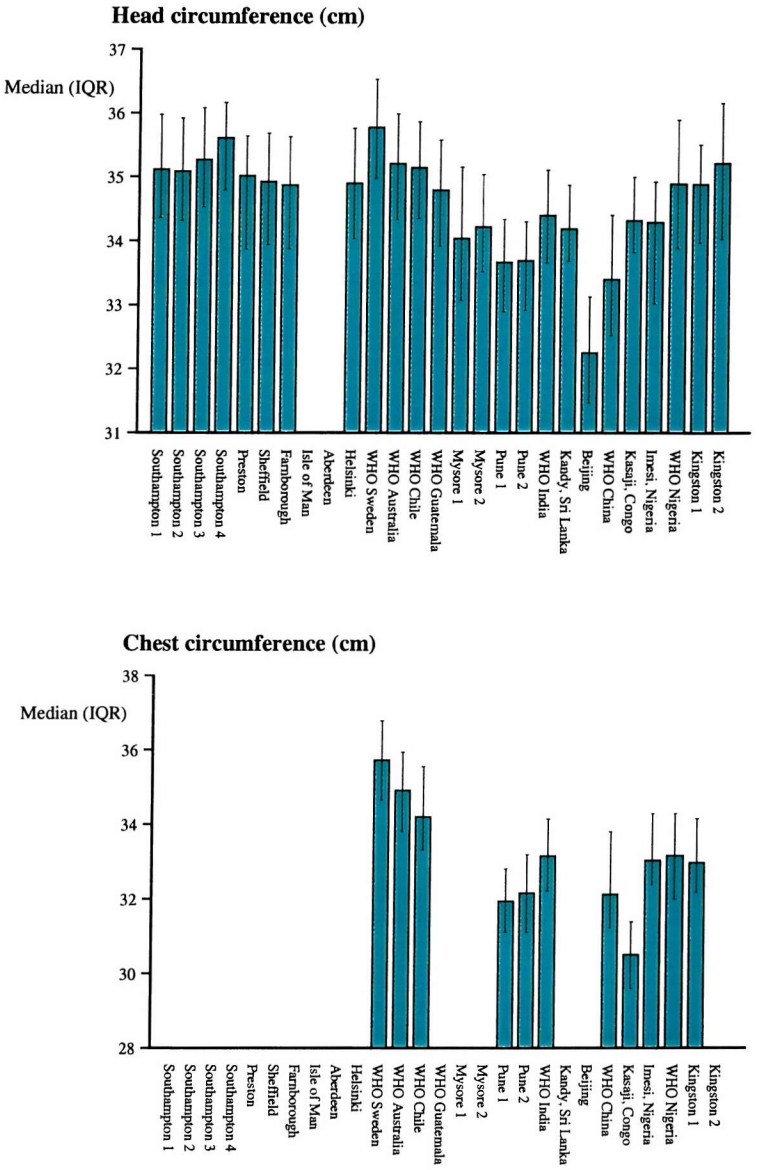
54.8% in Guatemala. Maternal age was calculated at delivery, and mothers were older in Sweden and Australia, and younger in Chile, Guatemala and India.

4.2.2 Size of neonates

Neonatal birthweight was no longer normally distributed in each dataset as it had been truncated at 2500g, and was dealt with appropriately in analyses. Bar charts that were constructed for the neonatal measurements available in the WHO datasets, all adjusted to 40 weeks gestation, are shown in Figure 4.13 (cf Figure 4.5 for the main datasets only). Tables of median values for the WHO datasets can be found in Appendix 2a.

Figure 4.13 Median (IQR) measurements - main and WHO study



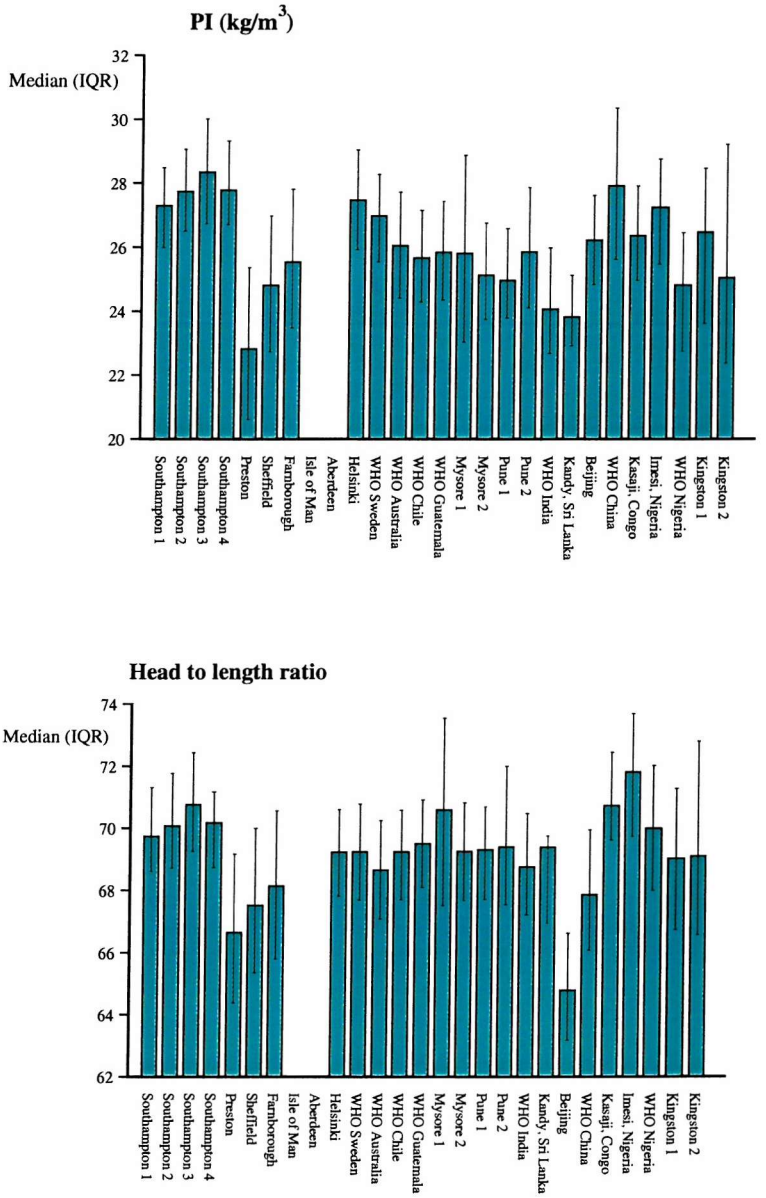


The WHO Swedish neonates were the largest in most dimensions. The WHO Australians were smaller than the Swedish, but of a similar size to the largest Europeans. The WHO Chileans were larger than the WHO Guatemalans, and were similar to the smallest Europeans.

Neonates from WHO India had similar values to those from Mysore 2 for all measurements. Chest circumference was similar for the WHO Nigerians and those from Imesi, although the WHO neonates were heavier and longer with bigger heads. The neonates from WHO China were heavier and shorter than those from Beijing. Their heads were bigger, although were still smaller than all other populations, even the other WHO datasets which were collected according to the same protocol.

Figure 4.14 shows the median values with IQRs for the variables derived from the direct measurements (cf Figure 4.6 for the main datasets only).

Figure 4.14 Median (IQR) derived measurements - main and WHO study



The WHO Swedish, Australian, Chilean and Guatemalan neonates were thinner than most of the other Europeans according to PI. The WHO Nigerians and Indians were substantially thinner, while the WHO Chinese were substantially fatter than those in the corresponding main study populations. The head sparing effect was less apparent in the WHO Indian and Nigerian datasets than the corresponding populations in the main study, using the head to length ratio. Neonates from WHO China had small heads compared to their lengths, although the ratio was higher than in Beijing.

Coefficients of variation are shown in Table 4.5, which compare the mean values across datasets for each neonatal measurement (cf Table 4.1 for the main datasets only).

Table 4.5 Coefficients of variation for each measurement – main and WHO study

Measurement	CV	SD (dataset means)	Overall mean
Birthweight (g)*	6.0%	24	3331
PI (kg/m^3)	5.2%	1.4	26.3
Chest (cm)	4.4%	1.5	33.7
Head (cm)	2.2%	0.7	34.6
CH length (cm)	2.2%	1.1	50.4
Head to length ratio (%)	2.0%	1.4	68.7

*Geometric mean and SD

CVs were ranked in the same order as Table 4.1, where only the datasets in the main study were considered. Each CV was now slightly reduced as expected, due the exclusion of low birthweight neonates. The only exception was chest circumference, which became more variable as a consequence of adding datasets from developed countries.

4.2.3 Shape of neonates

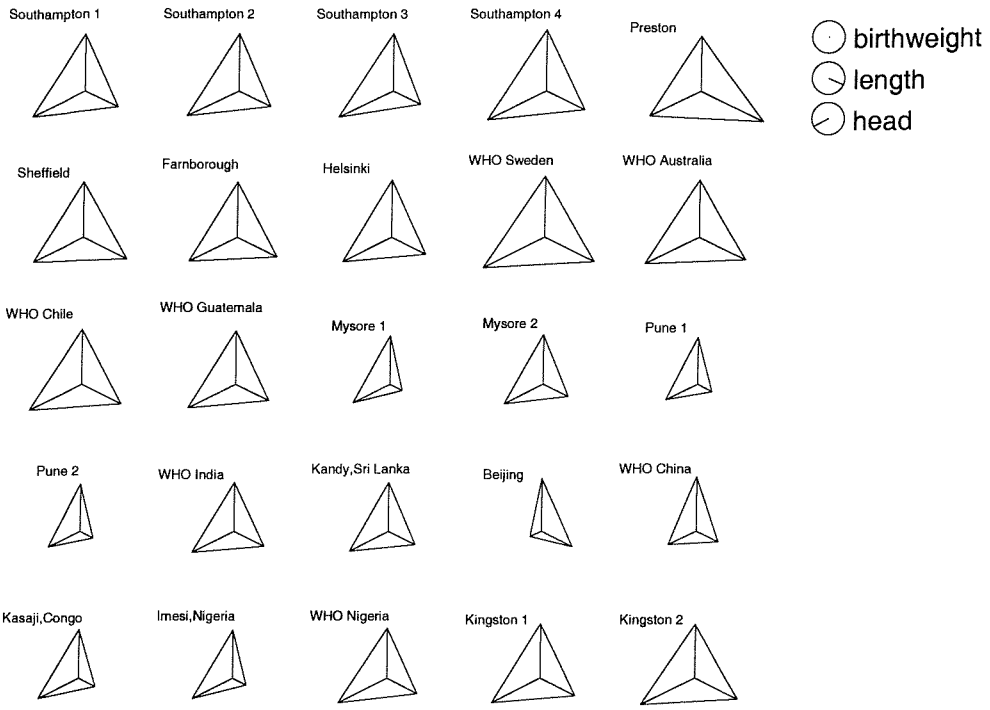
Star graphs were constructed using the same method as §4.1.3. Median values for birthweight, CH length and head circumference adjusted for gestation were used from each dataset. 'Smallest baby' values for the baseline were recalculated including the WHO datasets and restricted main datasets, and are shown in Table 4.6.

Table 4.6 Values used for star graph 'smallest baby' – main and WHO study

Variable	Minimum (of dataset medians)	SD (of dataset medians)	Minimum - SD
Birthweight (g)	2860.000	254.288	2605.712
CH length (cm)	48.154	1.173	46.967
Head circumference(cm)	32.247	0.779	31.468

The star graphs can be seen in Figure 4.15 (cf Figure 4.8 for the main datasets only).

Figure 4.15 Star graphs using birthweight, length and head circumference - main and WHO study



The neonates from WHO Sweden and Australia were the largest and fairly symmetrical. Those from WHO Chile and Guatemala were smaller but still symmetrical. In all the WHO Indian, Chinese and Nigerian populations, shapes were similar to the corresponding main study populations, although the distinction between head and length was less apparent.

4.3 Indices of adiposity

PI has been used as a measure of adiposity in analysis as more accurate measures such as skinfolds were only available in a small number of datasets. Obviously any adiposity index should be highly correlated with true measures of fatness. In addition, it is should be independent of length so that it does not have different meanings for short and long babies. As seen from Appendix 2c, the correlations between PI and CH length were significantly greater than zero in almost all populations. They ranged from 0.03 to 0.70 in absolute magnitude, and the greatest correlations were generally in the datasets from developing countries. Hence possible alternative measures of adiposity based only on ratios of birthweight and CH length were investigated.

4.3.1 Traditional indices

Weight for length (weight/length) has been used as an index of adiposity. Another common measure is the body mass index (BMI) proposed by Quetelet (1869). His rationale was that weight reflects volume, which involves more than one dimension, whereas length only reflects one dimension. He suggested that the ratio of weight and length squared should be used.

The PI, originally proposed by Livi (1897) goes one step further. He recognised that weight is a three-dimensional measure, so that if the body had the same form at different lengths, weight would be proportional to length cubed. Sheldon et al. (1940) and others have used an inverted version of this index. However, as body form does not remain constant for any given length, there are likely to be problems with this index.

Many studies have compared the performance of weight for height, BMI and PI (or inverted PI) as indicators of adiposity. However, these have all been based on children or adults rather than neonates. Keys et al. (1972) and others have shown that PI was the least satisfactory as it correlated with height and only moderately with fat. Weight for height and BMI both correlated highly with measures of fat or weight, but have not consistently been shown to be independent of height in all studies (for example Florey 1970). Billewicz et al. (1962) give examples of the potential for misleading results if an adiposity index is even moderately correlated with height, such as the appearance of trends with social class that may actually be due to height.

4.3.2 Alternative indices

Some attempts have been made to find a more appropriate index of adiposity using weight to height ratios. Khosla and Low (1967) and Benn (1971) both used theoretical approaches to develop formulae for calculating powers of height. These were based on minimising the correlation between the index and height. Khosla and Low fixed their index to be invariant along a regression of weight on height, so that the height power p could be calculated using:

$$p = \frac{\log W_b - \log W_a}{\log H_b - \log H_a}$$

where W = weight, H = height
a, b are any two points along the regression of weight on height.

Using data on more than 5000 men in Birmingham, they suggested that as p was equal to 1.94, it was acceptable to use BMI. However, any rounding of powers may sacrifice validity. BMI was highly correlated with weight, but not uncorrelated with height in all age groups in these data.

Benn used Taylor series expansion to derive an index that was approximately equivalent to relative weight based on a standard. The formula for the power is:

$$p = \beta \text{ (mean height / mean weight)}$$

where β is obtained from a regression of weight on height. He commented that an index using this power of height would also be correlated with adiposity provided height and adiposity were not correlated. Use of the 'Benn index' has shown it to be generally uncorrelated with height and correlated with weight or fat (Goldbourt and Medalie 1974, Lee et al. 1981, Garn and Pesick 1982). The major difficulty with this index is that it is population specific, so can only be used to compare individuals within the same population.

Abdel-Malek et al. (1985) proposed an index where powers were calculated for weight as well as height, but the main aim was to maximise correlation with fat. This index was based on regression in logarithmic form with percentage body fat as the outcome and weight and height as predictors. Using their data on 458 children and adults in the US, the index was calculated as $\text{weight}^{1.2}/\text{height}^{3.3}$. Although obviously it correlated highly with fat, it was also correlated with height in men. Micozzi et al. (1986) used this method (deriving their own power values) for their data on approximately 14,000 US adults and found there to be a correlation with height. Other problems with this index are that it will vary depending on the data, so is not comparable across populations, and a direct measure of fat is required in at least a subgroup of the population for calculations.

There has been very little published work on choice of adiposity index at birth. However, Cole et al. (1997) tried to find a suitable index that was uncorrelated with length. They commented that birthweight for length depended on gestation, and developed an index where the power of length changed linearly with gestation. It was derived from a regression of log weight on log length, including separate intercepts for each week of gestation, and the power was equal to the slope value. Using 999 neonates of at least 33

weeks gestation born in London, they calculated the index to be weight/length$^{2.6}$. Although this was uncorrelated with length, there was no comment regarding correlations with fat. As the index was again population specific, it was not possible to use it to compare across populations.

All these alternative indices are approximate, as linear relationships between height and weight (or fat and both height and weight for the Abdel-Malek method) must be assumed. Although this assumption may be reasonable, the variables will never be perfectly linearly related and so correlations between ratios using a power obtained by this method and height will not necessarily be zero.

4.3.3 New approach

Another approach based on exact rather than approximate methods was investigated which attempted to overcome some of the difficulties with the indices in §4.3.2. For each dataset, the optimal power for CH length (k) was chosen such that

$$\text{Correlation [(birthweight/CH length}^{k}\text{) and CH length] } = 0.$$

Gestation adjusted variables were used for calculations. The k values were derived using a gradient-based optimisation technique (Aoki 1971). For example, Figure 4.16 shows a range of k values plotted against the squared correlation between the birthweight to length ratio (based on the appropriate value of k) and length itself, for Southampton 1. The k value which minimises correlation with length is indicated (2.8).

Figure 4.16 Optimal power for length - Southampton 1

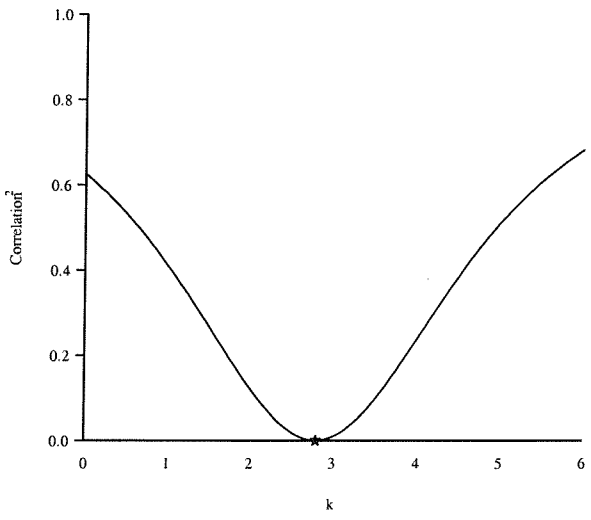


Table 4.7 shows the optimal power for length in each dataset. As a comparison, powers p calculated for the Benn index are also shown. Only the WHO datasets were restricted to neonates weighing at least 2500g.

Table 4.7 Optimal powers for length – minimum correlation with length

	k	p (Benn index)
Southampton 1	2.8	2.8
Southampton 2	2.7	2.7
Southampton 3	2.8	2.8
Southampton 4	2.3	2.2
Preston	1.6	1.5
Sheffield	1.5	1.6
Farnborough	1.3	1.3
Isle of Man	2.7	2.7
Helsinki	3.1	3.0
Mysore 1	1.0	1.0
Mysore 2	2.4	2.3
Pune 1	2.3	2.2
Pune 2	1.7	1.7
Kandy, Sri Lanka	2.9	2.8
Beijing	2.5	2.4
Kasaji, Congo	2.8	2.7
Imesi, Nigeria	2.2	2.2
Kingston 1	1.5	1.5
Kingston 2	1.2	1.1
WHO Sweden	2.1	2.1
WHO Australia	1.8	1.8
WHO Chile	2.2	2.2
WHO Guatemala	2.3	2.2
WHO India	1.4	1.4
WHO China	0.8	0.8
WHO Nigeria	1.4	1.4

The k values ranged from 0.8 to 3.1, and the lowest values corresponded to the strongest negative correlations between PI and length. Lower values tended to occur in datasets based on obstetric records, where CH length may have been over-measured (see §2.4.3), and also in datasets from the WHO study. Within the datasets based on clinic measurements, values in the UK and Sri Lanka were the highest, values in India, China and Africa were lower, and values in Jamaica the lowest of all. Similar k values were obtained if the sexes were considered separately, or if neonatal variables were used before they were adjusted for gestation.

Using the k values to calculate new indices, correlations with length were all less than 0.02 in absolute magnitude ($p \geq 0.4$ for all). If more decimal places had been used in calculations, correlations would be zero. The k values were all within 0.1 of those calculated for the Benn index.

For some datasets, it was possible to extend this analysis to calculate k values that maximise correlations of the new index with fat, as well as minimise correlations with length. Hence, the optimal power for length was chosen in each dataset such that

$$\text{Correlation [(birthweight/CH length}^k\text{) and CH length]} \approx 0 \qquad \text{and}$$

$$\text{Correlation [(birthweight/CH length}^k\text{) and fat]} \approx 1.$$

i.e. the following function required minimisation:

$$[\, w \times r_1^2 \,] + [\, (1 - w) \times (1 - r_2)^2 \,] \qquad \text{where } w = \text{weighting},$$

r_1 = correlation with length

r_2 = correlation with fat.

If equal weighting were given to fulfilling the two criteria, the function simplified to

$$[\, 0.5 \times r_1^2 \,] + [\, 0.5 \times (1 - r_2)^2 \,].$$

For example, Figure 4.17 shows a range of k values against this function for Southampton 3, with subscapular used as the direct measure of fat. Correlation with length was minimised and correlation with fat maximised when k took the value 2.5 as indicated.

Figure 4.17 Optimal power for length - Southampton 3

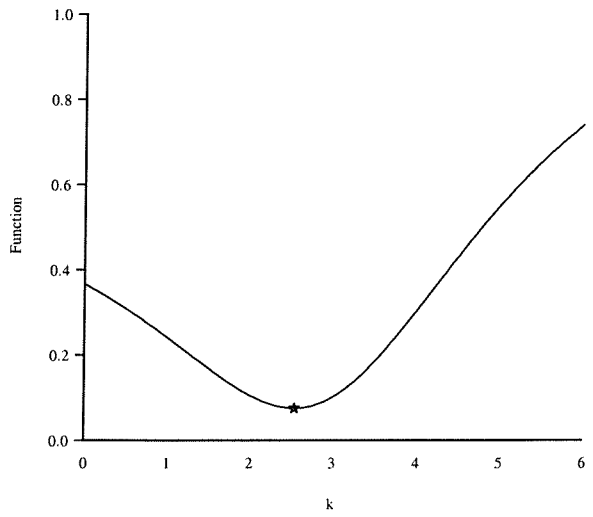


Table 4.8 shows the k values and resulting correlations with length and subscapular in each dataset. Results were within 0.1 of those shown if triceps replaced subscapular.

Table 4.8 Optimal powers for length – minimising correlation with length and maximising correlation with fat

	k	Correlation with length	Correlation with fat
Southampton 3	2.5	0.1	0.6
Mysore 2	2.1	0.1	0.6
Pune 1	2.0	0.1	0.5
Pune 2	1.4	0.1	0.6
Kasaji, Congo	2.4	0.2	0.5

All k values were lower than those based only on minimisation with length, i.e. even more different from the value three used for PI. Compared with PI, absolute correlations with length were reduced in most datasets, particularly India, and correlations with fat were increased as required, using the new indices. As maximising correlations with fat involved three variables, namely weight, length and fat, it was not possible to achieve values of one in each dataset (cf achieving exactly zero for correlations with length). Even if the function was weighted to give priority to maximising correlations with fat, the highest value obtained in any dataset was 0.7.

4.3.4 Conclusion

This new approach overcomes some of the difficulties with other alternative indices proposed in the literature. It is based on an exact rather than approximate method, and an index that is uncorrelated with length can be derived using only two measurements, weight and length. Correlations with fat can also be improved. However, the value of the CH length power varies across the datasets, which is not ideal. Hence PI had to be used for analysis, and results treated with caution.

4.4 Summary

Characteristics of datasets:

- There were similar proportions of males and females in each of the datasets. Gestational duration was shorter, there were a lower proportion of first borns, and mothers were younger in India and Africa, while the opposite was true in most of the UK datasets.

Size of neonates:

- Neonates in Europe and Australia had the largest values for most individual measurements, followed by those from the Jamaica, Chile, Guatemala and China, then Africa, India and Sri Lanka.
- There were wide variations in many of the measurements, although CR length, leg length and head circumference (after excluding Beijing where head size was markedly reduced) were relatively similar across the populations.
- Neonates from Beijing had short legs but long bodies, while those from Mysore 2 had short bodies but long legs.
- In Indian neonates, fat was less reduced than other measures of body composition, particularly muscle.
- There were no very low birthweight (< 2000g) neonates in Europe or China, and none with very high birthweight (> 4000g) in Pune, Sri Lanka or Kasaji.

Shape of neonates:

- When restricting consideration to birthweight, CH length and head circumference, the difference between populations was in the head to length ratio. Neonates in China had small head circumferences in relation to length, while head size was large compared to length in those from India, Sri Lanka and Africa. Adding placental weight did not alter this pattern.

Intercorrelations between measurements:

- There were positive correlations between all direct measurements, except leg length. Relationships for the ratio variables were less consistent across the datasets.

Sex, parity and maternal age differences in size and shape:

- Males were generally larger than females, although had less fat. First borns were smaller than subsequent births, and neonatal size increased as mothers became older. Differences were more marked in non-European countries. However, all neonates were similar shapes.

Indices of adiposity:

- PI was not an acceptable adiposity index. However, more appropriate alternatives required derivation within each population, and so were not comparable across populations.

5 Characterisation of maternal phenotypes

5.1 Choice of maternal variables

The following maternal measurements were selected for use in analysis:

- Height
- Body mass index (BMI)
- Head circumference
- Arm muscle area (AMA)
- Triceps skinfold
- Maternal birthweight.

In many of the datasets, the only available maternal measurements were height and weight. Height was of interest as it is thought to reflect childhood growth. BMI was selected in preference to weight. This was because weight depends on height i.e. taller women are heavier, and BMI was designed to measure soft tissue mass independently of height. Another possibility would have been to use 'relative weight', based on external standards. However, if reference weights were chosen for each population, the resulting indices would not be comparable across different populations. If the same reference weight were used for all populations to make results comparable, it would be difficult to find an appropriate population with high quality measurements to use and the same height-weight relationships would be assumed for the standard and all populations. Also, analysis with all six maternal variables would be inconsistent, as the other measurements would not be standardised.

BMI is a composite measure, including muscle and fat, and so individual measures of these components were also required. AMA was chosen to represent muscle. Mid-upper arm circumference (MUAC) alone could have been used, but this includes both fat and bone in addition to muscle in its measurement. AMA was designed to overcome these difficulties, and is based on a geometrical formula so is applicable to all populations. Another option would have been to use muscle mass, but this would have had the disadvantage of including height in the calculation. The triceps skinfold was chosen to represent fatness. Alternatives included other skinfolds, percentage body fat and fat mass. Triceps were chosen in preference to the other skinfolds as it is one of the easiest to

measure, the techniques of measurement have been well standardised, and it was available in more datasets than the others. Also, this skinfold measured peripheral fat, indicative of the general level of fatness, which was preferable to a measure of central fat which is more indicative of the distribution of fat. Calculating both percentage body fat and fat mass required use of equations derived from Western populations, so may not be appropriate for many of the datasets used in the analysis. Another disadvantage of using fat mass was that weight was required for calculation.

Head circumference was of interest as it is thought to represent the mother's growth in infancy. Maternal birthweight was also of interest as a reflection of the mother's own intrauterine experience.

If measurements were available at more than one timepoint during pregnancy, the 30-week value was used. There were several reasons for this. Very few of the datasets had pre-pregnant measurements and of these, all except one were self-reported so would have been less accurate, so this timepoint was not suitable. Although a number of the datasets had measurements at 37-weeks, this would not have been the ideal measurement to use as the fetus itself would have a large influence on the mother's weight by this time. The same number of datasets had measurements recorded at both 20 and 30-weeks. Both Southampton 4 and the Isle of Man only had one set of measurements which spanned wide ranges of gestations, so choice of timepoint was less relevant to these. However, Mysore 2 only had measurements at 30-weeks. It was important to include this dataset as all the maternal variables of interest were recorded, and fieldworkers were specifically trained to take the measurements so the data were of a relatively high quality. Also, within each dataset that had antenatal data recorded, the 30-week data were more complete as many women did not book till later in their pregnancy.

The datasets from Preston and Sheffield were not included in this analysis as none of the maternal variables of interest had been measured. The only maternal variable that could be used in Helsinki and the seven WHO datasets was height, as no others had been recorded at appropriate timepoints. Similarly height and head were the only measurements which could be used in Pune 2. These datasets were included in this chapter where possible, although any analyses involving combinations of maternal variables could not be undertaken.

Each of the datasets in these analyses were restricted to mother-baby pairs where at least some information on the mother's size was recorded. Table 5.1 shows the numbers of mother-baby pairs within each dataset that were used.

Table 5.1 Numbers used for analysis

Dataset	Number	% of original dataset excluded
Southampton 1	557	0.0%
Southampton 2	521	0.0%
Southampton 3	376	0.3%
Southampton 4	102	0.0%
Farnborough	1677	0.0%
Isle of Man	388	0.0%
Aberdeen	233	0.0%
Helsinki	5979	0.2%
Mysore 1	1071	13.4%
Mysore 2	597	0.0%
Pune 1	633	0.0%
Pune 2	258	4.1%
Kandy, Sri Lanka	446	2.0%
Beijing	2421	0.5%
Kasaji, Congo	338	0.0%
Imesi, Nigeria	266	1.1%
Kingston 1	489	0.2%
Kingston 2	66	5.7%
WHO Sweden	505	0.0%
WHO Australia	622	0.0%
WHO Chile	688	0.0%
WHO Guatemala	294	0.0%
WHO India	504	0.0%
WHO China	541	0.0%
WHO Nigeria	512	0.0%

In a few of the datasets there were some non-random missing values. In Mysore 1 height was only recorded after 1952 so just under a quarter were missing, and antenatal weights were only recorded until 1990 so just under half were missing. In both Mysore 1 and Mysore 2, maternal birthweight was only recorded if the mother had been born in the hospital in which the datasets were collected. This meant that just under two thirds in Mysore 1 and approximately 90% in Mysore 2 were missing. In Kasaji, MUAC and tricep skinfold measurements were only recorded from 1997 onwards, so just under half the mothers had missing values for these variables.

In each of these datasets, there were no significant differences in maternal body composition and age between those that had other anthropometric measurements recorded

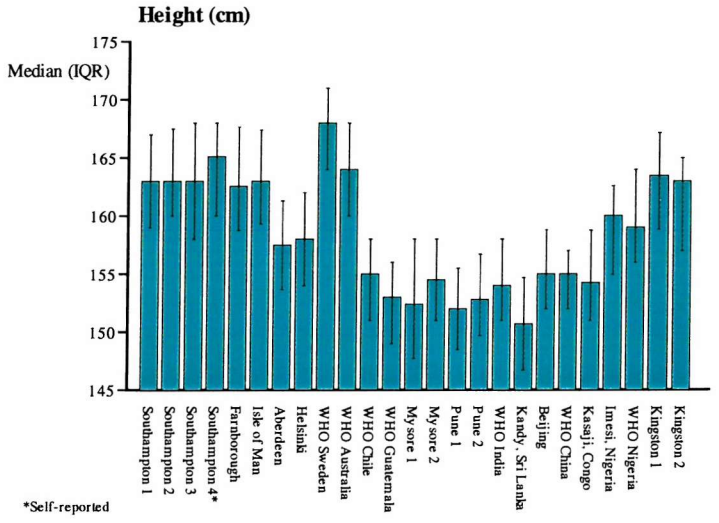
and those that did not. However, a higher proportion of mothers in Mysore 1 with data recorded for both height and their own birthweight were primiparous.

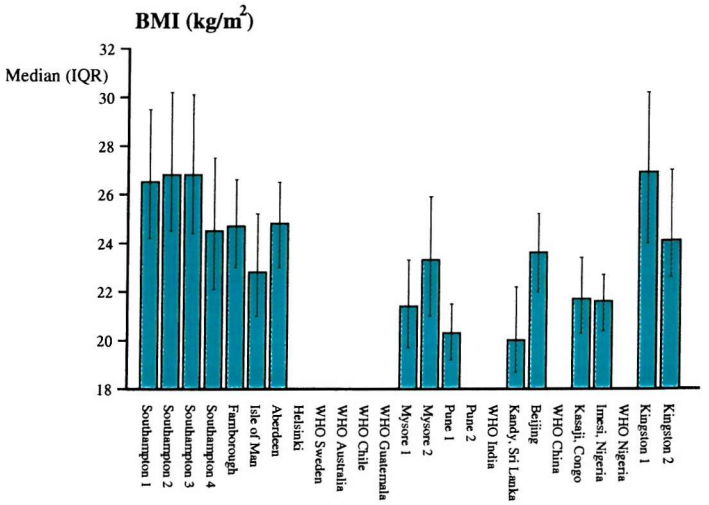
5.2 Size of mothers

Maternal birthweight, adult height and head circumference were normally distributed in all datasets. 30-week BMI, AMA and triceps skinfold had skewed distributions in each of the datasets, and so were dealt with appropriately in analysis.

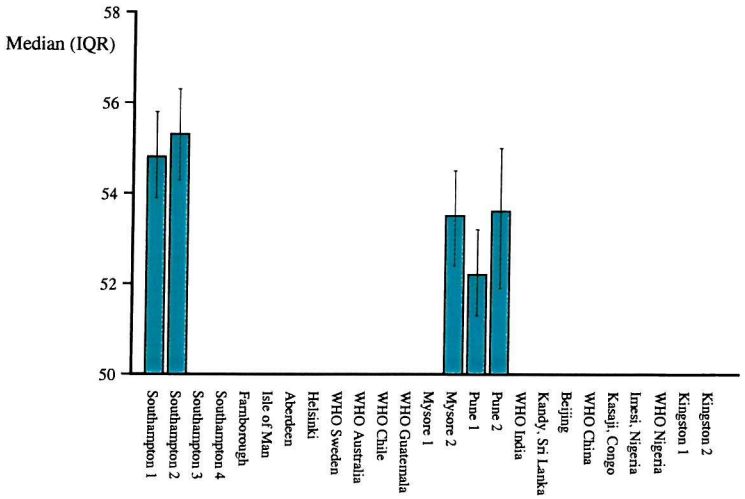
Figure 5.1 shows the median values with IQRs for the measurements of interest in each dataset. Tables of median values can be found in Appendix 3a.

Figure 5.1 Median (IQR) measurements

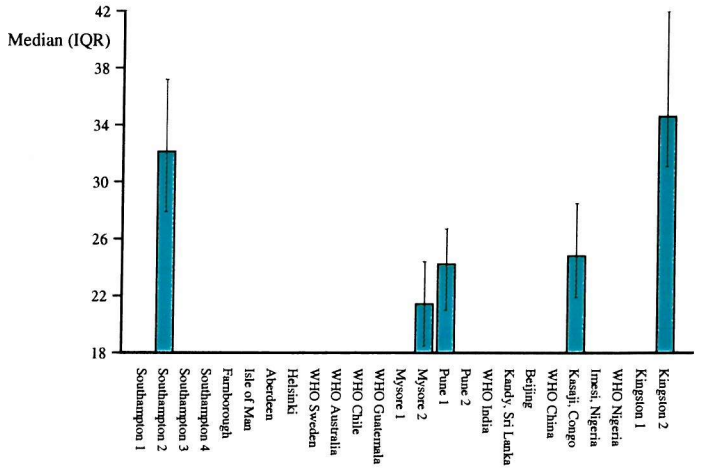




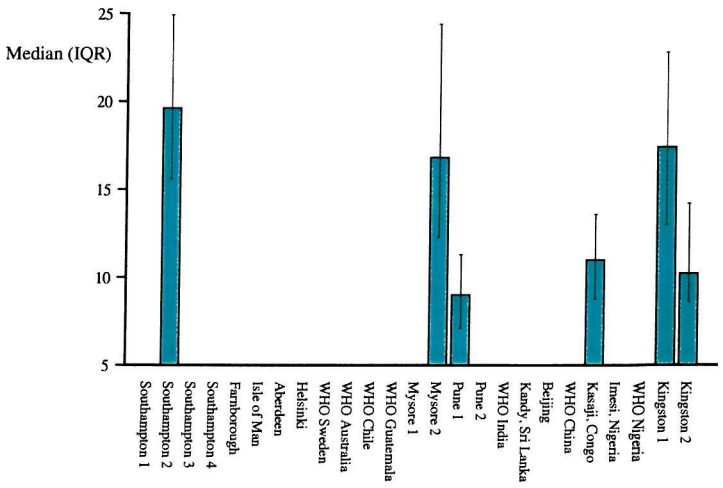
Head circumference (cm)

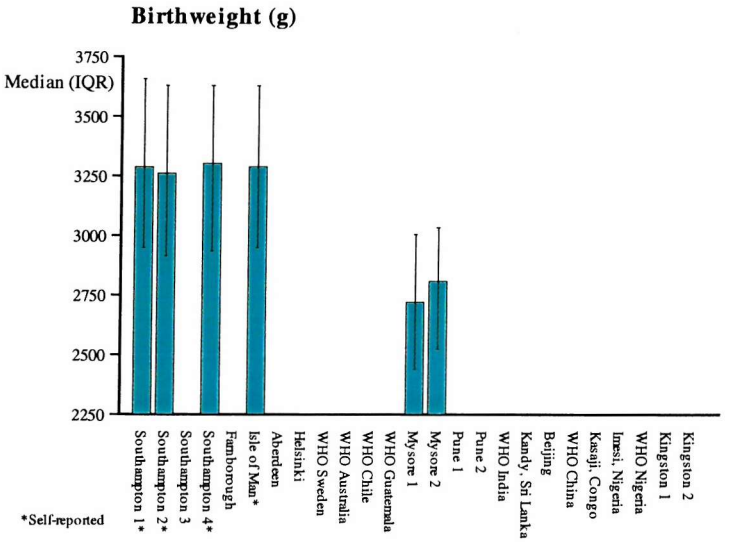


AMA (cm^2)



Triceps (mm)





European, Jamaican and Australian mothers were the largest in all measurements. These were followed by the Chinese, Central and South Americans, and Africans. The Indians and Sri Lankans were the smallest of all.

Within the European populations the Swedish mothers were the tallest and the Southampton mothers had the highest BMIs. Mothers from Kingston 1 were taller with higher BMIs than those from Kingston 2. In Africa the mothers from Nigeria were substantially taller than those from Kasaji, though their BMIs were similar. Mysore mothers were slightly taller and had larger heads than those from Pune. They were much fatter, although they had less muscle. Sri Lankan mothers were slightly smaller than those from Pune.

The mother's birthweights were compared with those of their offspring using paired t-tests. Mean differences (offspring – mother) are shown in Table 5.2 for males and females separately and together. P-values for the significance of the differences are also given.

Table 5.2 Differences in neonatal and maternal birthweights

	Male		Female		Male and female		
	Diff (g)	p-value	Diff (g)	p-value	Diff (g)	p-value	N
Southampton 1	201	<0.001	49	0.2	131	<0.001	506
Southampton 2	295	<0.001	122	0.007	210	<0.001	476
Southampton 4	357	0.003	338	0.001	347	<0.001	84
Isle of Man	209	0.001	135	0.004	172	<0.001	303
Mysore 1	269	<0.001	129	0.001	207	<0.001	412
Mysore 2	220	0.02	129	0.1	160	0.008	63

For the sexes together, there were significant increases between the generations in all datasets, varying from 130g to 350g. Differences for male offspring were greater than those for female offspring in all datasets. Gestation could not be taken into account for this analysis, as it was not recorded for the mothers.

Coefficients of variation were used to compare the mean values across the datasets for each measurement. These were derived by dividing the SD of the mean values from each dataset by the overall mean value, and multiplying by 100.

Results are shown in Table 5.3, where variables are shown in descending order of CVs to aid interpretation.

Table 5.3 Coefficients of variation for each measurement

Measurement	CV	SD (dataset means)	Overall mean
Triceps (mm)	29.5%	4.7	16.1
AMA (cm^2)	24.2%	6.4	26.3
BMI (kg/m^2)	10.2%	2.5	24.3
Birthweight (kg)	7.9%	247	3131
Height (cm)	3.1%	4.9	158.0
Head (cm)	2.6%	1.4	53.8

Adult fat and muscle measurements were the most variable between populations, while the skeletal measurements were the least variable.

5.3 Shape of mothers

The following combinations were used for this analysis, as not all variables were measured in all datasets:

1) Height, BMI

These variables were chosen as they were available in most of the datasets.

2) Height, head circumference, AMA, triceps

The separate components of body mass were of interest, namely skeleton, muscle and fat, and were available in some of the datasets.

3) Height, AMA, triceps

Both Kasaji and Kingston 2 included measures of muscle and fat, although head circumference had not been recorded in either dataset.

4) Maternal birthweight, height, head circumference, AMA, triceps

In Southampton 2 and Mysore 2, maternal birthweight was available in addition to the adult variables already mentioned.

Star graphs and principal components analysis were used to investigate the geographical variation in maternal phenotypes. Star graphs were based on median values of the measurements from each dataset. However, if these values had been used for the PCA, there would have been too few observations to allow principal components to be derived for sets of variables involving head circumference or maternal birthweight, which were only measured in a small number of datasets. Hence individual values were pooled to derive the coefficients for the components. PC scores for each subject were then calculated, checked for normality, and then the mean scores within each dataset were based on these.

Star graphs

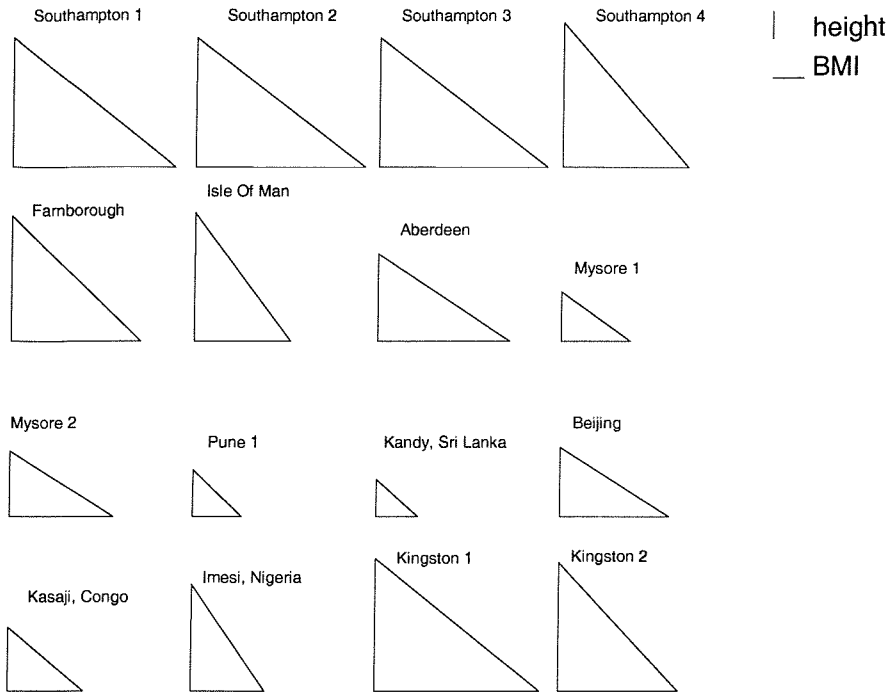
Star graphs were drawn using the method of §4.1.3, with the lengths of the rays of the stars proportional to the relative magnitudes of the measurements. As for the neonates, a 'smallest mother' was constructed using the minimum value minus SD for each measurement. These values were derived from the dataset of median values in each population and are shown in Table 5.4.

Table 5.4 Values used for star graph 'smallest mother'

Variable	Minimum (of dataset medians)	SD (of dataset medians)	Minimum - SD
Height (cm)	150.700	5.000	145.700
BMI (kg/m^2)	19.923	2.292	17.631
Head (cm)	52.200	1.557	50.623
AMA (cm^2)	21.412	5.630	15.782
Triceps (mm)	8.951	4.651	4.300
Birthweight (g)	2806.590	320.609	2485.981

In the first set of stars (Figure 5.2), the vertical ray represents height and the horizontal ray represents BMI.

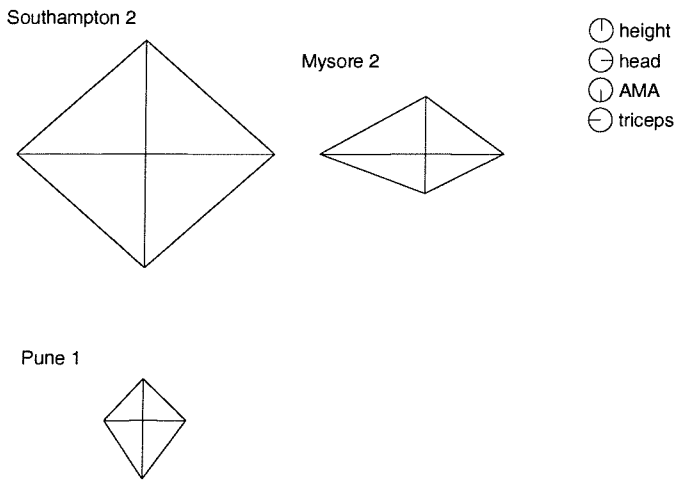
Figure 5.2 Star graphs using height and BMI



The largest mothers were seen in Europe and Jamaica. They were all of a similar shape, except that the mothers in Aberdeen were slightly shorter. The rest of the mothers were smaller. Those in Mysore and Beijing were relatively short, while those in Imesi were relatively tall and thin. Those in Pune, Kandy and Kasaji were all short and thin.

Figure 5.3 shows star graphs for the second model; height is represented by the ray pointing up, head by the ray pointing right, AMA by the ray pointing down, and triceps the ray pointing to the left.

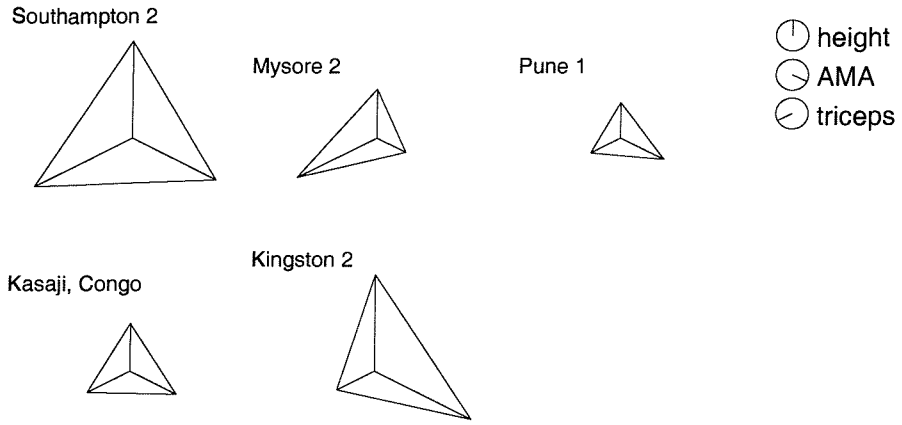
Figure 5.3 Star graphs using height, head, AMA and triceps



The Southampton mothers were the largest, followed by those from Mysore and then Pune. Mysore mothers were relatively fat, while the Pune mothers were relatively muscular.

Star graphs for the third model are shown in Figure 5.4.

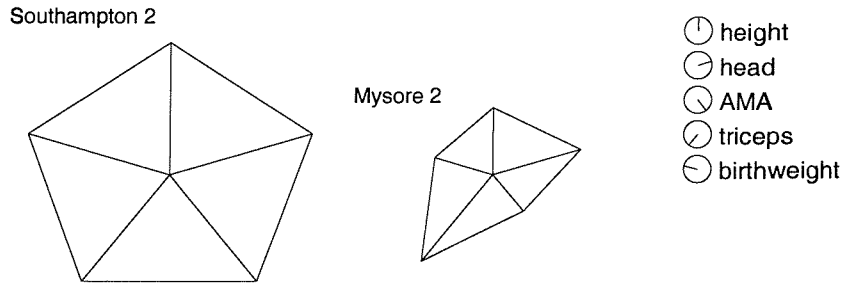
Figure 5.4 Star graphs using height, AMA and triceps



Similar conclusions for Southampton, Mysore and Pune can be drawn as for Figure 5.3. The mothers in Kingston were relatively tall and muscular, but had reduced tricep measurements. The Kasaji mothers were relatively small in all dimensions.

The fourth model is shown in Figure 5.5.

Figure 5.5 Star graphs using height, head, AMA, triceps and maternal birthweight



Introducing maternal birthweight made little difference to the overall shape of the mothers. The Southampton mothers remained symmetric, while those in Mysore were smaller in all dimensions except for triceps skinfold.

Principal components analysis

PCA was carried out for three of the sets of variables; this method is uninformative when based on just two variables so was not used for height and BMI.

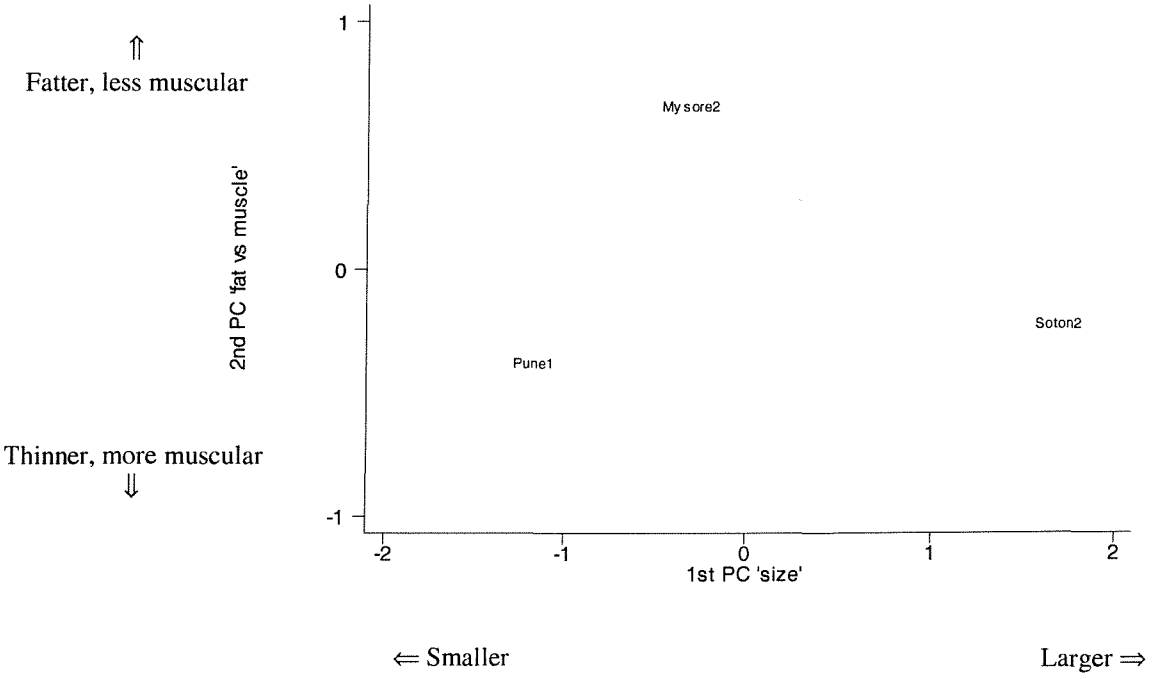
For height, head circumference, AMA and triceps, the first PC accounted for 57% of the variation in the data, and the first two PCs for 77%. The coefficients for these PCs are shown in Table 5.5.

Table 5.5 Principal components using height, head, AMA and triceps

Original variable	PC1	PC2
Height	0.53	-0.23
Head	0.56	0.07
AMA	0.47	-0.56
Triceps	0.43	0.79

The first PC reflected the overall size of the mother. In the second PC, the coefficients for AMA and triceps were of a similar size although had opposite signs, while the coefficients for height and especially head were relatively small. This could be interpreted as a contrast between fat and muscle, with higher values on this PC representing mothers with more fat relative to muscle. Figure 5.6 shows the plot of the first two components.

Figure 5.6 Principal components using height, head, AMA and triceps



Mothers in Mysore had more fat relative to muscle compared to the other datasets. Mothers in Pune had the least fat relative to muscle, although were not substantially different those from Southampton on this component.

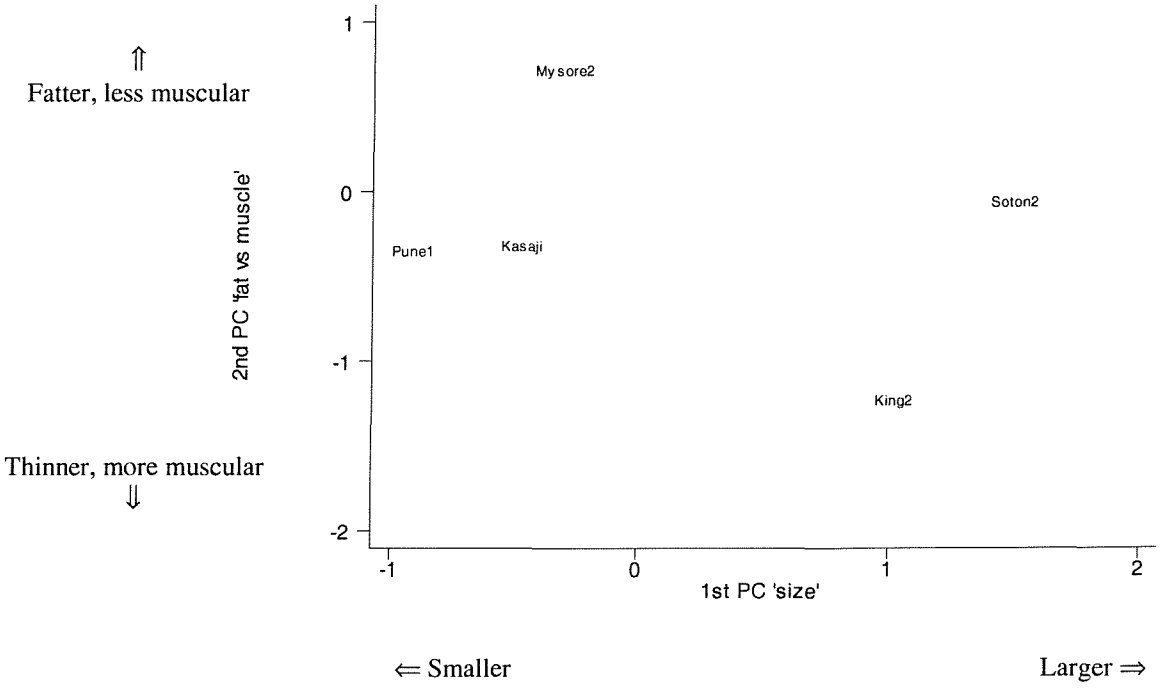
For the third model, the first PC accounted for 55% of the variation, and the first two for 82% of the variation in the data. Coefficients are shown in Table 5.6.

Table 5.6 Principal components using height, AMA, triceps

Original variable	PC1	PC2
Height	0.63	-0.21
AMA	0.60	-0.48
Triceps	0.49	0.85

The first PC reflected overall maternal size. The second PC was still a contrast between fat and muscle as the coefficient for height was relatively small. Figure 5.7 shows the plot of these components.

Figure 5.7 Principal components using height, AMA and triceps



The amount of fat relative to muscle was highest in Mysore, similar in Southampton, Pune and Kasaji, and lowest in Kingston.

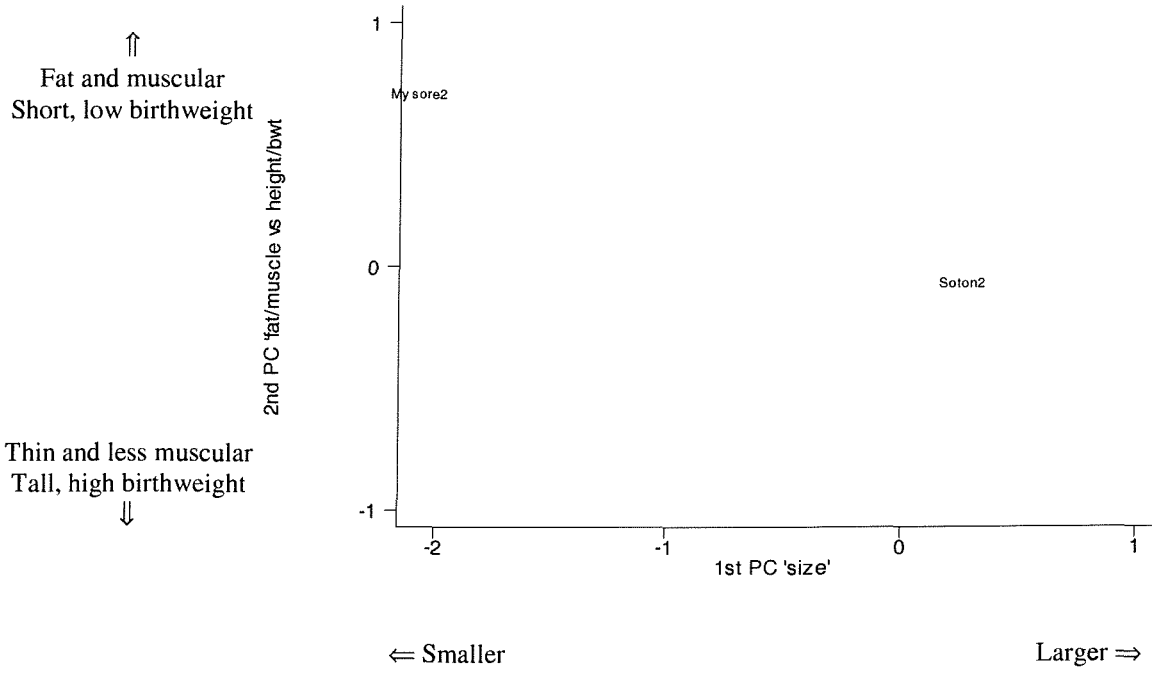
For the final model, the first PC accounted for 41% of the variation, and the first two for 63% of the variation in the data, and coefficients are shown in Table 5.7.

Table 5.7 Principal components using height, head, AMA, triceps and maternal birthweight

Original variable	PC1	PC2
Height	0.49	-0.43
Head	0.53	-0.10
AMA	0.48	0.38
Triceps	0.32	0.72
Birthweight	0.39	-0.37

The first PC again reflected overall maternal size. The second PC was a contrast of fat and muscle against height and birthweight. High values on this coefficient suggested that the mother had a relatively low birthweight and was short, fat and muscular. These findings are illustrated in Figure 5.8.

Figure 5.8 Principal components using height, head, AMA, triceps and maternal birthweight



Mysore mothers had higher values than those from Southampton on the second component. This was probably dominated by their high tricep measurements as this variable contributed the most to this component.

5.4 Intercorrelations between measurements

It was important to understand how the maternal variables were related to each other before using them to investigate mother to baby relationships. Correlation coefficients were calculated between the maternal variables available within each of 16 datasets, using individual values. Spearman correlation coefficients were used as BMI, AMA and triceps skinfold had skewed distributions. Results can be seen in Table 5.8, coloured according to size ($|r|<0.10$ $0.10\leq|r|\leq0.20$ $|r|>0.20$ $|r|$ = absolute correlation).

Table 5.8 Spearman correlation coefficients

	Southampton 1	Southampton 2	Southampton 3	Southampton 4	Farnborough	Isle of Man	Aberdeen	Mysore 1	Mysore 2	Pune 1	Pune 2	Kandy, Sri Lanka	Beijing	Kasaji, Congo	Imesi, Nigeria	Kingston 1	Kingston 2
Height/BMI	-0.03	-0.20	-0.06	-0.09	-0.11	0.01	0.06	-0.41	-0.07	-0.01		-0.10	-0.20	0.12	0.04	-0.07	0.07
Height/head	0.29	0.34							0.30	0.21	0.27						
Height/AMA		0.11							0.06	0.23				0.34			0.40
Height/triceps		-0.05							0.08	0.13				0.07		-0.03	-0.03
Height/birthweight	0.29	0.23		0.26		0.28		0.21	0.28								
BMI/head	0.31	0.21							0.34	0.20							
BMI/AMA		0.63							0.33	0.43				0.66			0.71
BMI/triceps		0.80							0.81	0.54				0.57		0.84	0.76
BMI/birthweight	0.09	0.09		-0.02		0.16		0.16	0.07								
Head/AMA		0.24							0.17	0.20							
Head/triceps		0.16							0.30	0.12							
Head/birthweight	0.25	0.22							0.09								
AMA/triceps		0.34							-0.03	-0.03				0.25			0.43
AMA/birthweight		0.04							0.03								
Triceps/birthweight		0.11							0.17								

In general there were consistent positive relationships between the following:

- Height and head circumference
- Height and AMA
- Height and maternal birthweight
- BMI and head circumference
- BMI and AMA
- BMI and triceps
- Head circumference and AMA
- Head circumference and triceps
- Head circumference and maternal birthweight
- Triceps and maternal birthweight.

The relationship between AMA and maternal birthweight was not significant in either of the datasets in which it was possible to investigate this.

The following relationships were inconsistent across the datasets:

- Height and BMI were not correlated except for significant negative relationships in Southampton 2, Farnborough, Mysore 1 and Beijing
- Height and triceps were not correlated except in Pune 1
- BMI and maternal birthweight were weakly correlated in some European datasets but not elsewhere
- AMA and triceps were significantly positively related in all datasets except India.

5.5 Indices of adiposity

In §4.3, the possible inadequacies of traditional indices of adiposity such as BMI were discussed. As seen from Table 5.8, correlations between BMI and height in the mothers were not more than 0.2 in absolute magnitude in any dataset except in Mysore 1 where the value was –0.41. However, it was of interest to see if this index could be improved upon, using an optimisation procedure as in §4.3.3.

For each dataset, a power for height, k, was chosen such that

Correlation [(weight/height^k) and height] = 0.

Table 5.9 shows the optimal power for height in each dataset. Powers for the Benn Index (Benn 1971) were calculated for comparison.

Table 5.9 Optimal powers for height – minimum correlation with height

	k	p (Benn index)
Southampton 1	1.8	1.8
Southampton 2	1.2	1.2
Southampton 3	1.7	1.7
Southampton 4	1.8	1.9
Farnborough	1.6	1.6
Isle of Man	1.9	1.8
Aberdeen	2.2	2.2
Mysore 1	0.7	0.7
Mysore 2	1.6	1.6
Pune 1	1.9	1.9
Kandy, Sri Lanka	1.7	1.7
Beijing	1.4	1.4
Kasaji, Congo	2.3	2.3
Imesi, Nigeria	2.1	2.1
Kingston 1	1.8	1.8
Kingston 2	2.3	2.3

The k values ranged from 0.7 to 2.3, although most could be rounded to 2, the value used for BMI. The k values were all within 0.1 of those calculated for the Benn index.

This analysis could be extended to allow for maximisation of correlations with fat as well as minimisation of correlations with height in six of the datasets. Table 5.10 shows the k values and resulting correlations with height and triceps in each dataset.

Table 5.10 Optimal powers for height – minimising correlation with height and maximising correlation with fat

	k	Correlation with height	Correlation with fat
Southampton 2	1.3	0.0	0.8
Mysore 2	1.6	0.0	0.8
Pune 1	1.8	0.0	0.6
Kasaji, Congo	2.2	0.0	0.6
Kingston 1	1.8	0.0	0.8
Kingston 2	2.3	0.0	0.8

K values were very similar to those obtained previously, and hence correlations with height remained zero. Compared with BMI, correlations with fat were only slightly higher using the new indices.

Therefore, as these alternative indices were not comparable across populations, and were actually very similar to BMI in most datasets, this traditional index was acceptable to use as a measure of adiposity for the mothers.

5.6 Summary

Size of mothers:

- European and Jamaican mothers were generally the largest in most measurements, while those from India and Sri Lanka were the smallest.
- There was wider variation in adult fat and muscle than skeletal measurements across the populations.

Shape of mothers:

- The main difference between mothers was in the amount of fat relative to muscle. Mysore mothers were relatively fat while mothers from Kasaji, Pune and particularly Kingston were relatively muscular.

Intercorrelations between mothers:

- The measurements were correlated with each other except for height and BMI, height and triceps, BMI and birthweight and also AMA and birthweight in most populations.

Indices of adiposity:

- BMI was found to be an acceptable measure of adiposity in each population, after comparison with other possible measures based on height and weight.

6 Mother to baby relationships

Relationships of maternal to neonatal anthropometry were analysed using various techniques. First however, it was necessary to examine the effects of possible confounders in these relationships, and also check for linearity, as this was assumed for some of the analyses.

Associations between maternal and neonatal measurements were firstly compared across datasets using regression. Within each dataset, the effects of each maternal measurement on the different neonatal measures were compared, as were the effects of different maternal measurements on each neonatal measure, again using regression.

The extent to which geographical differences in neonatal phenotypes were explained by differences in their mother's phenotype was then examined. If maternal body composition could not explain the neonatal differences, then other factors must be involved. Two methods were used to investigate this. Firstly, variations in maternal phenotype were adjusted for and then neonates compared, to look for location effects. Secondly, neonates born to mothers of similar sizes were compared to see if location effects were specific to certain maternal phenotypes.

6.1 Confounders in mother to baby relationships

Maternal age and parity, neonatal sex and gestational duration may have affected the maternal variables, neonatal variables or both, and so these relationships were investigated.

6.1.1 Relationships between confounders

Spearman correlations were used to compare relationships between maternal age, parity (in five groups, 0, 1, 2, 3, 4 or more, analysed as a continuous variable) and gestational duration within each dataset. Maternal age and parity were highly significantly related, with $p<=0.001$ for all datasets. Stronger correlations were seen in the non-European countries, Africa in particular, where the proportion of higher parity mothers was relatively high. Maternal age and gestation were negatively correlated in many of the datasets, as were parity and gestation. However, correlations were relatively weak.

Distributions of maternal age, parity and gestation were compared between the sexes using Mann Whitney and chi-squared tests. There were no significant differences.

6.1.2 Effect of confounders on maternal anthropometry

The effects of maternal age and parity on the maternal variables (height, 30-week BMI, head, 30-week AMA and 30-week triceps) were investigated using regression. Log transformations were used where required. Parity was grouped into 0, 1, 2, 3, 4+, although it was analysed as a continuous variable as before. Individual relationships between both age and parity with the maternal measurements were assessed using F tests. Cubic terms and higher were not included as they were considered not to be biologically plausible. The simultaneous effects of age and parity were also considered, and interaction terms tested for significance. Datasets were restricted to mother-baby pairs where both age and parity were recorded to ensure individual and simultaneous effects were comparable. Appendix 4a shows the linear regression coefficients and, if appropriate quadratic coefficients for individual models, and also the linear coefficients for the simultaneous models. Coefficients are colour coded according to the strength of their significance. Maternal birthweight, and the possible confounders gestational duration and neonatal sex were excluded from this analysis, as relationships were unlikely.

Older women were taller in some datasets, although in others, the tallest mothers were those in the middle of the age distributions, or there were no relationships, occurring mainly in developing countries. Older women were fatter according to both BMI and triceps skinfold in most datasets. However, there were quadratic relationships (in both directions) in some datasets. Older women were more muscular, although mothers in the middle of the age distribution were the most muscular in a few of the datasets. There were no relationships between maternal age and head circumference in any of the datasets.

Maternal height was related to parity in several of the datasets, and the direction of the relationships was usually negative. Women with higher parities were fatter according to BMI and triceps skinfold in many datasets, although there were some quadratic relationships (in both directions). There were positive relationships between parity and AMA in all datasets. Parity did not have an effect on head circumference in any of the datasets.

Effects of maternal age and parity on height, which generally acted in opposite directions, were strengthened after simultaneous adjustment, although were lost in Africa. Positive effects on BMI, triceps and AMA were weakened in most datasets, particularly for parity. The lack of relationships with head circumference remained after adjustment. There were very few significant interactions between maternal age and parity. Those that existed were weak, and likely to have occurred by chance due to the large number of tests that have been undertaken.

6.1.3 Effects of confounders on neonatal anthropometry

The effects of maternal age, parity, neonatal sex and gestation on the 16 neonatal measurements were investigated using the same method as §6.1.2, and results are shown in Appendix 4b. Placental weight has been omitted for Mysore 1 throughout this chapter, as there were only five neonates with this measurement who also had their mother's measurements recorded.

Older women had larger babies, particularly in the developing countries. Higher parity was also associated with larger babies, although generally not related to length. There were no relationships between either maternal age or parity and the neonatal ratio variables (excluding PI) in most datasets. Relationships between neonatal sex and the anthropometric measurements have been summarised in §4.1. Neonates with longer gestations were generally larger, although relationships between gestation and the neonatal ratio variables were generally negative.

Effects of maternal age and parity generally remained similar or were weakened after simultaneous adjustment for the other confounders. Boys remained larger than girls for most measurements except fat, and gestation still had a positive effect on most measurements after adjustment. Again, there were only a small number of interactions between the confounders, which were likely to have occurred by chance.

6.2 Linearity of mother to baby relationships

Linearity of the relationships between each maternal measurement and each neonatal measurement was assessed using F tests (Appendix 4c). Adjustments were made for neonatal sex and gestation.

Positive linear relationships existed between most of the direct neonatal measurements (i.e. all except ratios) and maternal height, BMI, head circumference and birthweight in the majority of the datasets. Both maternal AMA and triceps were either positively or not related to the neonatal measures in most of the datasets. The maternal variables were generally not related to the neonatal ratio variables, although there were some weak negative relationships.

6.3 Geographical variation in mother to baby relationships

Associations between measurements in each dataset were investigated using several approaches. Selected results from these methods are presented to illustrate important points.

6.3.1 Individual mother to baby relationships

In a series of separate graphs for each maternal-neonatal pair, regression lines were plotted for each dataset. F tests were used to investigate whether the maternal-neonatal relationships in each dataset could be represented by a common slope and intercept. Neonatal variables were adjusted for gestation where possible. The length of each regression line was limited to the range of maternal measurements recorded. This analysis assumed linearity between the maternal variables for simplicity, which has been shown to be acceptable in most cases (§6.2).

Table 6.1a shows whether each maternal-neonatal relationship could be represented by a common slope, with p-values colour coded according to significance. The number of datasets used for each analysis is shown in brackets. Table 6.1b shows the range of estimates if separate slopes were required, or the common slope estimate if there were no significant differences in slopes. The latter were derived from models that included indicator variables for each dataset.

Table 6.1a Common slopes test for each maternal-neonatal pair of measurements

p≥0.1 p<0.1 p<0.05 p<0.01

	Maternal variable P-value for common slope *(number of datasets)*					
Neonatal variable	Height	BMI	Head	AMA	Triceps	Birthweight
Birthweight	<0.001*(25)*	<0.001*(16)*	0.5*(5)*	0.01*(5)*	0.7*(6)*	0.2*(6)*
Placental weight	0.2*(16)*	0.02*(14)*	0.1*(5)*	0.2*(5)*	0.7*(6)*	0.3*(6)*
CH length	<0.001*(24)*	<0.001*(15)*	0.9*(5)*	0.001*(5)*	0.1(6)	0.6*(6)*
CR length	0.7*(7)*	0.004*(7)*	0.97*(4)*	0.06*(3)*	0.01*(4)*	0.02*(4)*
Leg length	0.4*(7)*	0.04*(7)*	0.5*(4)*	0.05*(3)*	0.3*(4)*	0.7*(4)*
Head	0.03*(24)*	0.06*(15)*	0.6*(5)*	0.04*(5)*	0.5*(6)*	0.06*(6)*
Chest	0.7*(11)*	0.3*(4)*	0.3*(2)*	<0.001*(2)*	0.2*(3)*	*(0)*
Abdomen	0.05*(9)*	0.01*(8)*	0.2*(5)*	0.08*(3)*	0.6*(4)*	0.01*(5)*
MUAC	0.05*(9)*	0.06*(8)*	0.8*(5)*	0.2*(4)*	0.7*(5)*	0.01*(4)*
AMA	0.01*(4)*	0.3*(3)*	0.9*(3)*	0.08*(3)*	0.7*(3)*	*(0)*
Triceps	0.3*(4)*	0.6*(3)*	0.1*(3)*	0.9*(3)*	0.2*(3)*	*(0)*
Subscapular	0.5*(5)*	0.3*(4)*	0.9*(3)*	0.7*(3)*	0.08*(3)*	*(0)*
PI	<0.001*(25)*	<0.001*(15)*	0.1*(5)*	0.2*(5)*	0.03*(6)*	0.05*(6)*
Head/length	0.02*(25)*	0.03*(15)*	0.4*(5)*	0.1*(5)*	0.2*(6)*	0.4*(6)*
Head /abdomen	0.5*(9)*	0.2*(8)*	0.01*(5)*	0.99*(3)*	0.1*(4)*	0.2*(5)*
Placenta /birthweight	0.3*(16)*	0.9*(14)*	0.3*(5)*	0.8*(5)*	0.7*(6)*	0.1*(6)*

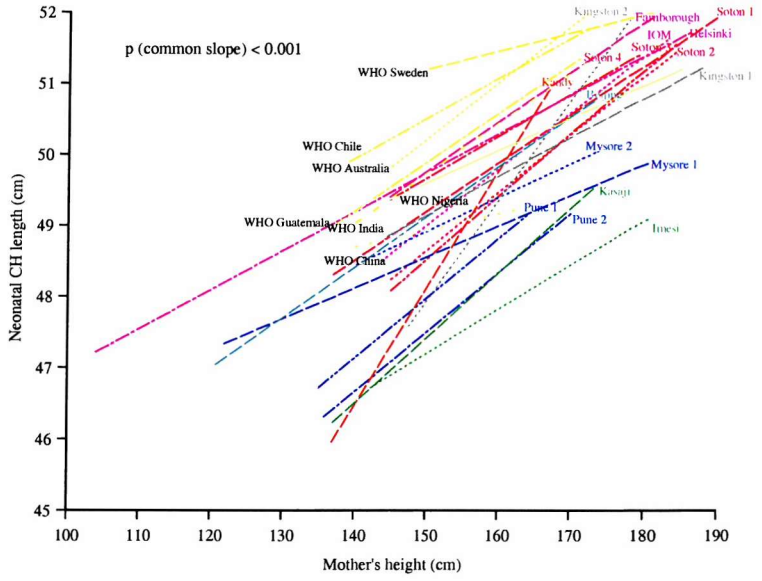
Table 6.1b Slope estimates for each maternal-neonatal pair of measurements

	Maternal variable Slope estimates					
Neonatal variable	Height (cm)	BMI (kg/m^2)	Head (cm)	AMA (cm^2)	Triceps (mm)	Birthweight (kg)
Birthweight (g)	6.55 to 20.74	15.83 to 55.62	44.14	3.86 to 25.26	11.8	196.6
Placental weight (g)	1.84	1.93 to 14.48	7.17	1.24	2.00	25.59
CH length (cm)	0.04 to 0.17	0.003 to 0.42	0.19	-0.004 to 0.12	0.04	0.61
CR length (cm)	0.04	-0.03 to 0.10	0.14	0.001 to 0.04	-0.03 to 0.06	0.41 to 1.47
Leg length (cm)	0.03	-0.01 to 0.11	0.03	-0.005 to 0.04	0.01	0.13
Head (cm)	0.01 to 0.07	-0.03 to 0.15	0.17	0.002 to 0.06	0.03	0.16 to 1.21
Chest (cm)	0.04	0.11	0.16	-0.01 to 0.10	0.04	
Abdomen (cm)	0.01 to 0.09	0.03 to 0.14	0.15	-0.002 to 0.04	0.04	0.13 to 1.49
MUAC (cm)	0.005 to 0.04	0.04 to 0.07	0.07	0.01	0.02	0.29 to 1.07
AMA (cm^2)	0.01 to 0.08	0.13	0.16	0.01 to 0.08	0.03	
Triceps (mm)	0.01	0.01	0.02 to 0.09	0.01	0.02	
Subscapular (mm)	0.01	0.06	0.04	0.01	0.0001 to 0.02	
PI (kg/m^3)	-0.05 to 0.05	-0.06 to 0.28	-0.05 to 0.20	0.03	-0.04 to 0.08	0.66
Head/length (%)	-0.13 to –0.01	-0.59 to 0.14	0.07	0.02	0.01	-0.23
Head /abdomen (%)	-0.05	-0.06	-0.40 to 0.29	0.02	-0.05	-0.66
Placenta /birthweight (%)	-0.01	0.03	0.02	0.01	0.01	-0.09

Maternal height

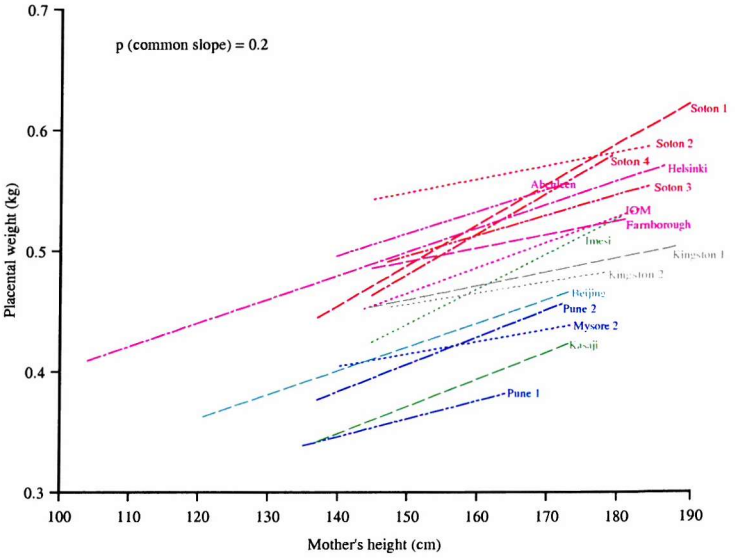
For some of the neonatal outcomes, relationships with maternal height could not be represented by a common slope for all datasets. This was generally due to stronger relationships in the developing countries. For example, the relationship between maternal height and CH length is shown in Figure 6.1.

Figure 6.1 Maternal height and CH length



However, common slopes could adequately represent the relationships between maternal height and placental weight, CR and leg length, chest circumference, fat, head to abdomen and placenta to birthweight ratios. Figure 6.2 shows the relationship with placental weight.

Figure 6.2 Maternal height and placental weight

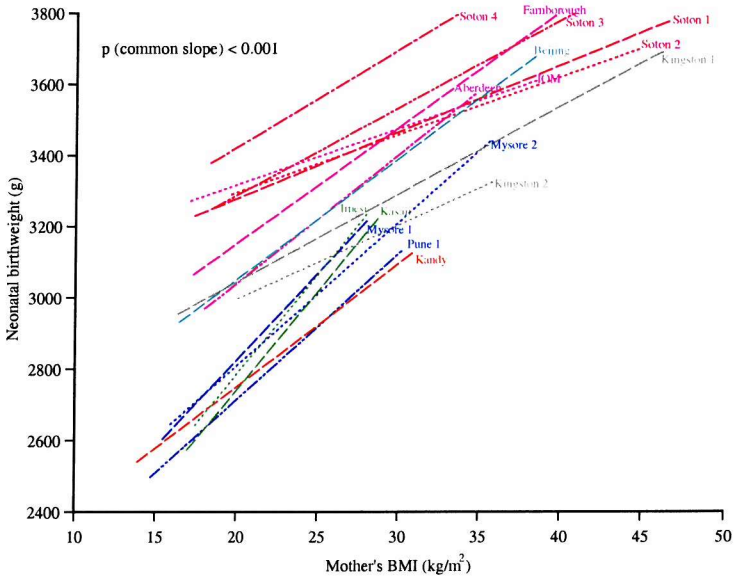


Maternal BMI

For relationships with maternal BMI, different slopes were required for many of the neonatal outcomes. This was again generally due to stronger relationships in the developing countries. For example, maternal BMI had a stronger effect on neonatal

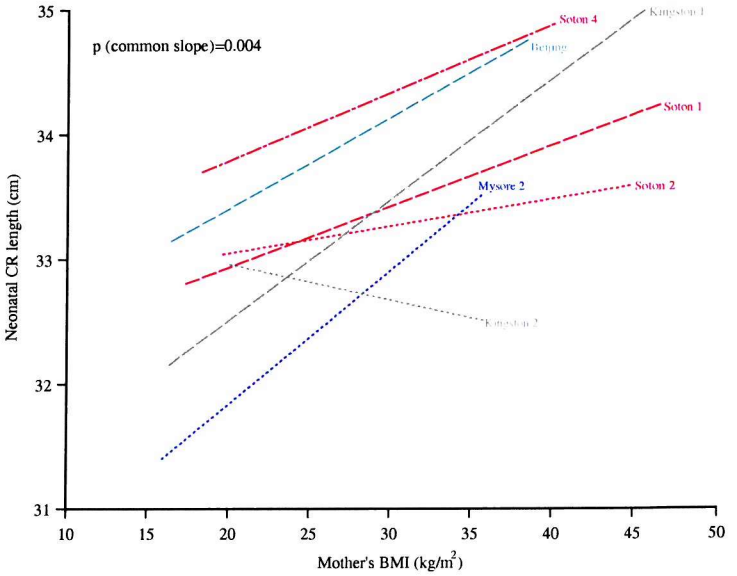
birthweight in India, Sri Lanka, China and Africa (Figure 6.3), although within these countries relationships were similar.

Figure 6.3 Maternal BMI and neonatal birthweight



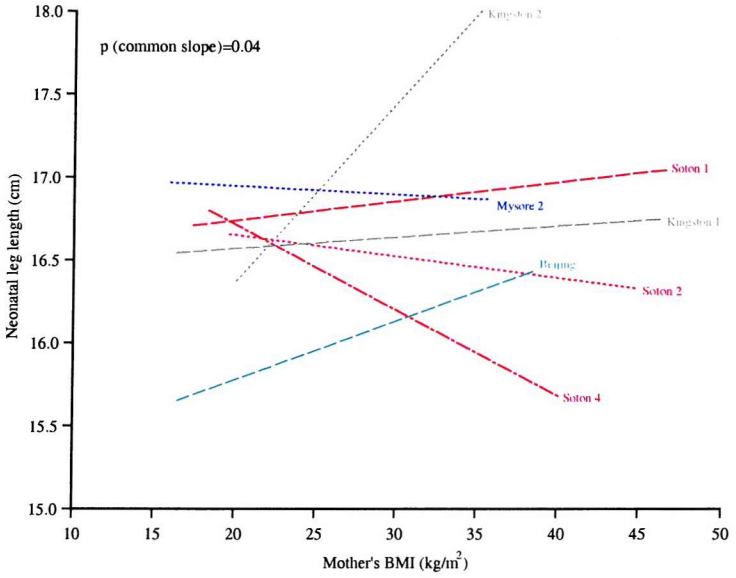
Separate slopes were required for both CR length and leg length, mainly due to differing relationships in Kingston 2. There was a marked positive effect of maternal BMI on CR length in all datasets except Kingston 2, where the effect was negative (Figure 6.4).

Figure 6.4 Maternal BMI and CR length



In contrast, maternal BMI had a strong positive effect on leg length in Kingston 2, but little effect in the other datasets (Figure 6.5).

Figure 6.5 Maternal BMI and leg length

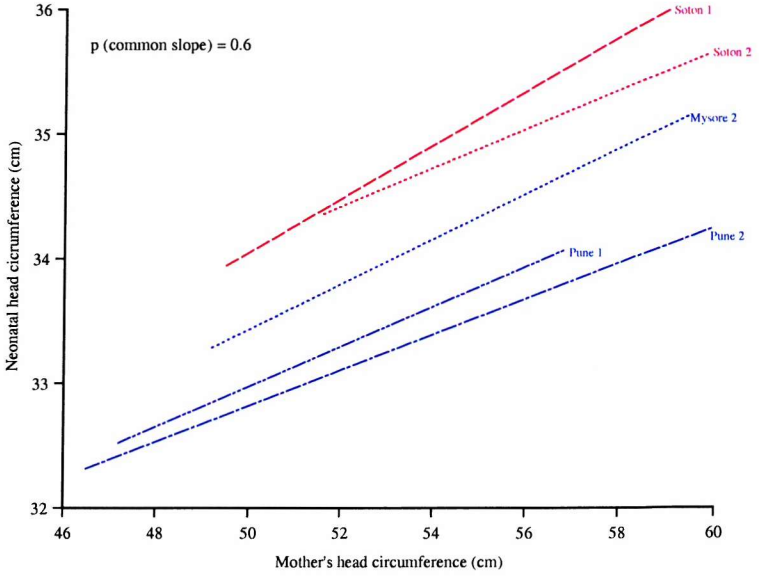


Common slopes were adequate for relationships between maternal BMI and neonatal chest circumference, muscle, fat, head to abdomen and placenta to birthweight ratios.

Maternal head circumference

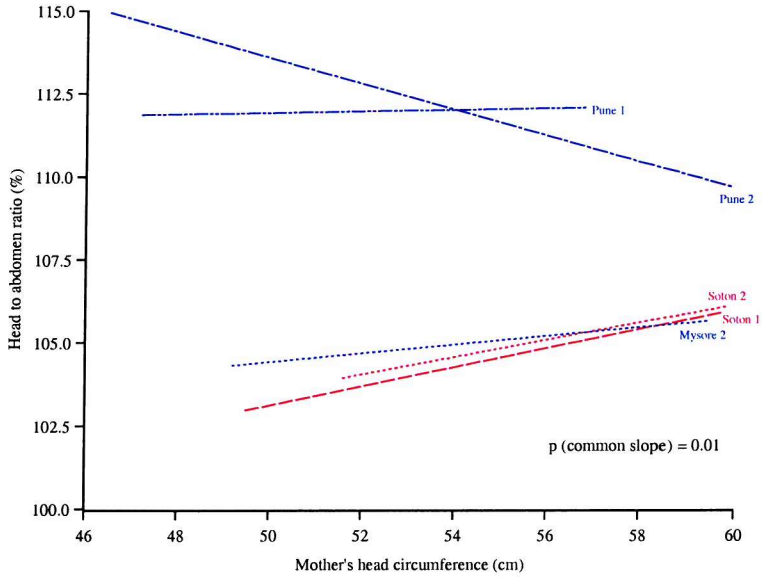
A common slope could describe most relationships with maternal head. For example, Figure 6.6 shows the effect of maternal head on neonatal head across the datasets.

Figure 6.6 Maternal head circumference and neonatal head circumference



The only exception was the head to abdomen ratio, where there were negative relationships with maternal head in Pune 2, and positive relationships elsewhere (Figure 6.7).

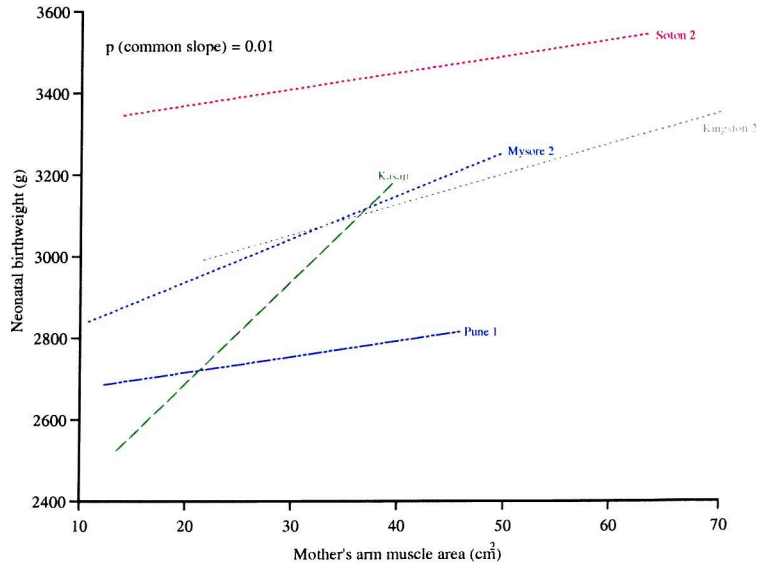
Figure 6.7 Maternal head circumference and head to abdomen ratio



Maternal AMA

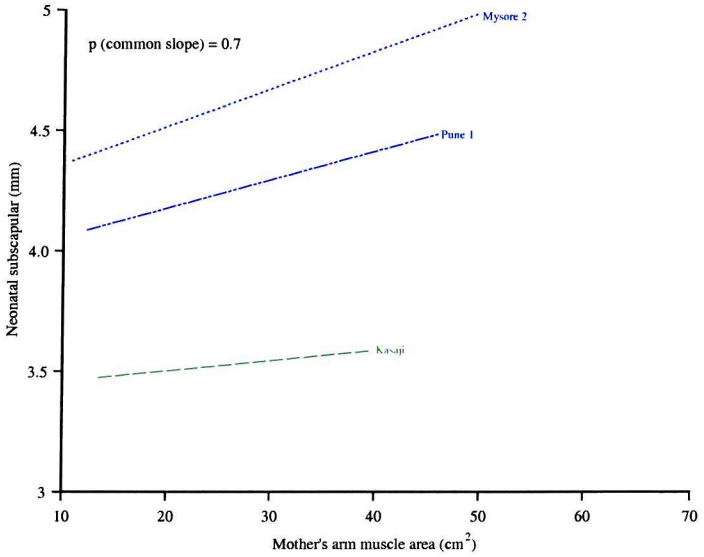
Relationships between maternal AMA and neonatal birthweight, length, head and chest circumference varied across the datasets. For these variables, there were much stronger relationships in Kasaji than the other datasets. Figure 6.8 shows the relationship with neonatal birthweight.

Figure 6.8 Maternal AMA and neonatal birthweight



For all other relationships with maternal AMA, common slopes were adequate. For example, Figure 6.9 shows the relationships with neonatal subscapular across the datasets.

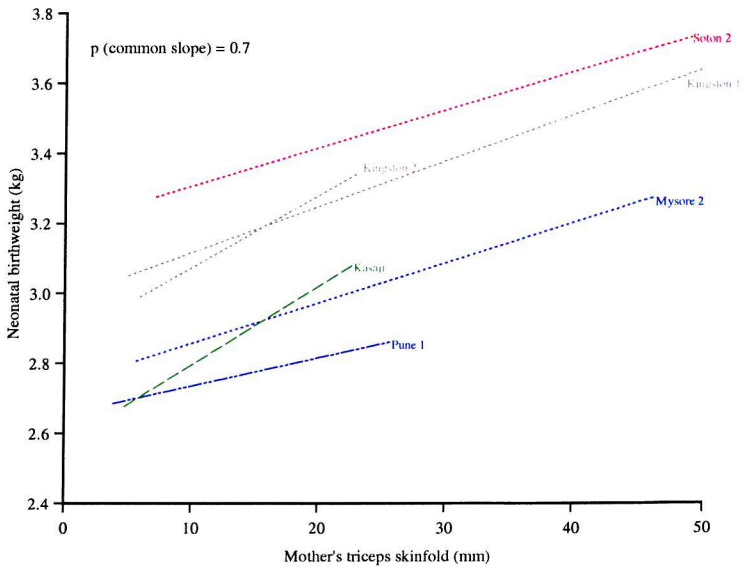
Figure 6.9 Maternal AMA and neonatal subscapular



Maternal triceps

Common slopes were acceptable for almost all relationships between maternal triceps skinfold and neonatal variables. For example, the relationship between maternal triceps and neonatal birthweight was similar across the datasets as shown in Figure 6.10.

Figure 6.10 Maternal triceps and neonatal birthweight



However, there were differences in relationships with CR length and leg length (not significant), and patterns were similar to those seen for maternal BMI. Maternal triceps had a strong positive effect on CR length, except in Kingston 2 where the effect was negative (Figure 6.11). However, there were no relationships with leg length except in Kingston 2 where maternal triceps had a positive effect (Figure 6.12).

Figure 6.11 Maternal triceps and CR length

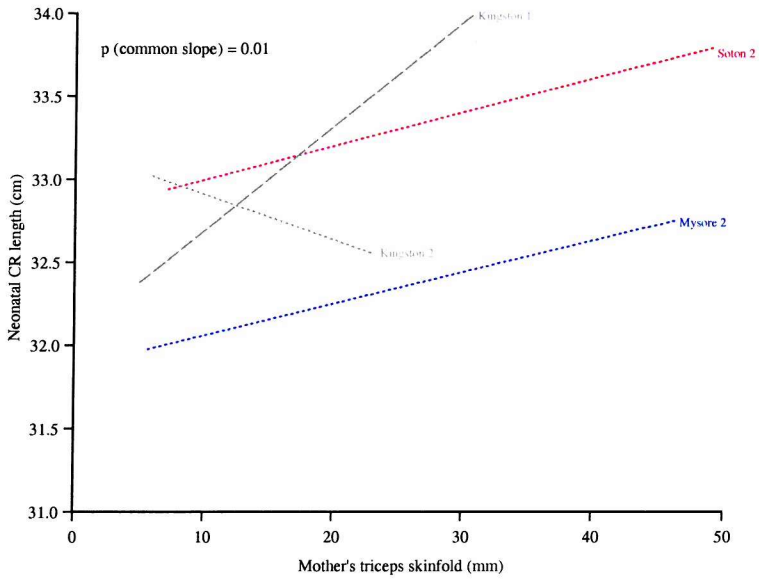
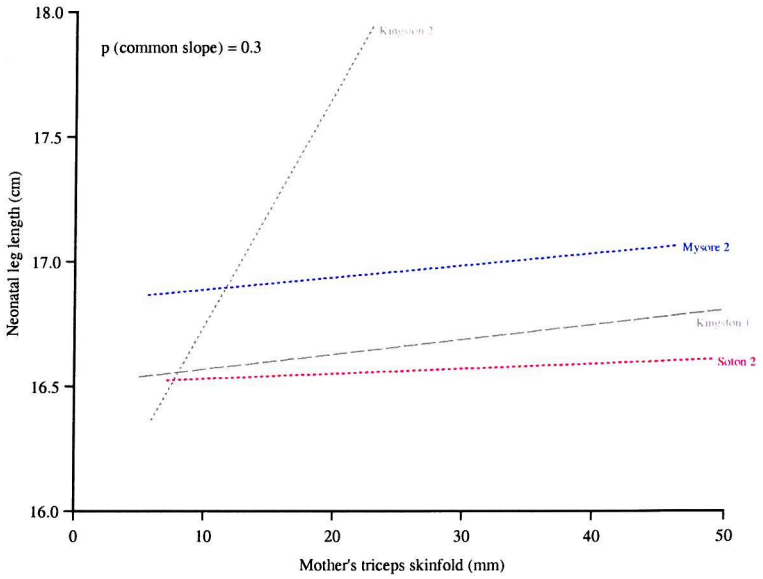


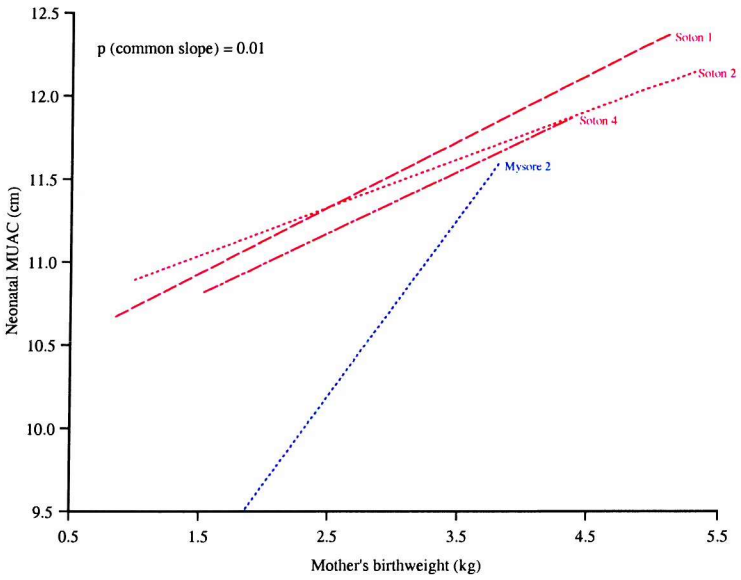
Figure 6.12 Maternal triceps and leg length



Maternal birthweight

Relationships between maternal birthweight and the neonatal variables differed between the Southampton datasets and Mysore 2 for CR length, head, abdominal and mid-upper arm circumferences. Figure 6.13 shows the relationship with neonatal MUAC.

Figure 6.13 Maternal birthweight and neonatal MUAC



For all neonatal variables the effect of maternal birthweight was stronger in Mysore 2 than the Southampton datasets.

For all relationships between maternal and neonatal variables where a common slope was adequate, different intercepts were required for each dataset. In general, similar results were obtained if adjustment was also made for sex, maternal age at delivery and parity. If the 30-week values were replaced by those obtained before pregnancy or at 20- or 37-week gestation where avaliable, relationships with neonatal variables were similar.

6.3.2 Comparison across neonatal measurements

The effects of each maternal measurement on the different neonatal measures were compared within each dataset. The effect of an SD score increase in the maternal variable was illustrated as an SD score change in each neonatal measure using regression, where

$$\text{SD score} = \frac{\text{individual value} - \text{dataset mean}}{\text{dataset SD.}}$$

Logged variables were used in calculations for maternal BMI, AMA and triceps. All effects were adjusted for neonatal sex and gestation. Results for individual maternal variables are presented, although adjustments for other maternal variables using the four combinations outlined in §5.3 were also investigated. Figures 6.14a and b compare the effects of each of the six maternal variables across all the neonatal measures for Southampton 2 and Mysore 2 respectively.

The maternal variables generally had positive effects on all the direct neonatal measures. Effects on the ratio variables were inconsistent across the datasets, but were often negative, and usually small except for PI. For all the maternal variables, there were relatively strong effects on neonatal birthweight in all datasets. In addition, there were also stronger effects of maternal height on neonatal length, maternal BMI and maternal head on neonatal head, and maternal birthweight on neonatal muscle. Maternal height, head and birthweight all had relatively weak effects on placental weight. Maternal height also had weaker effects on neonatal fat, as did maternal BMI and triceps skinfold on neonatal length, leg length in particular.

Similar patterns were seen when adjustments were made for other maternal variables. With or without adjustment, the widest variation in the SD changes across neonatal measurements was generally seen for maternal birthweight. The least variation was generally seen for maternal AMA. The widest ranges of neonatal absolute SD scores were seen in Mysore and Kasaji, while the narrowest ranges were seen in Southampton and Pune for most neonatal measures.

Figure 6.14a Effects of maternal variables on neonatal variables – Southampton 2

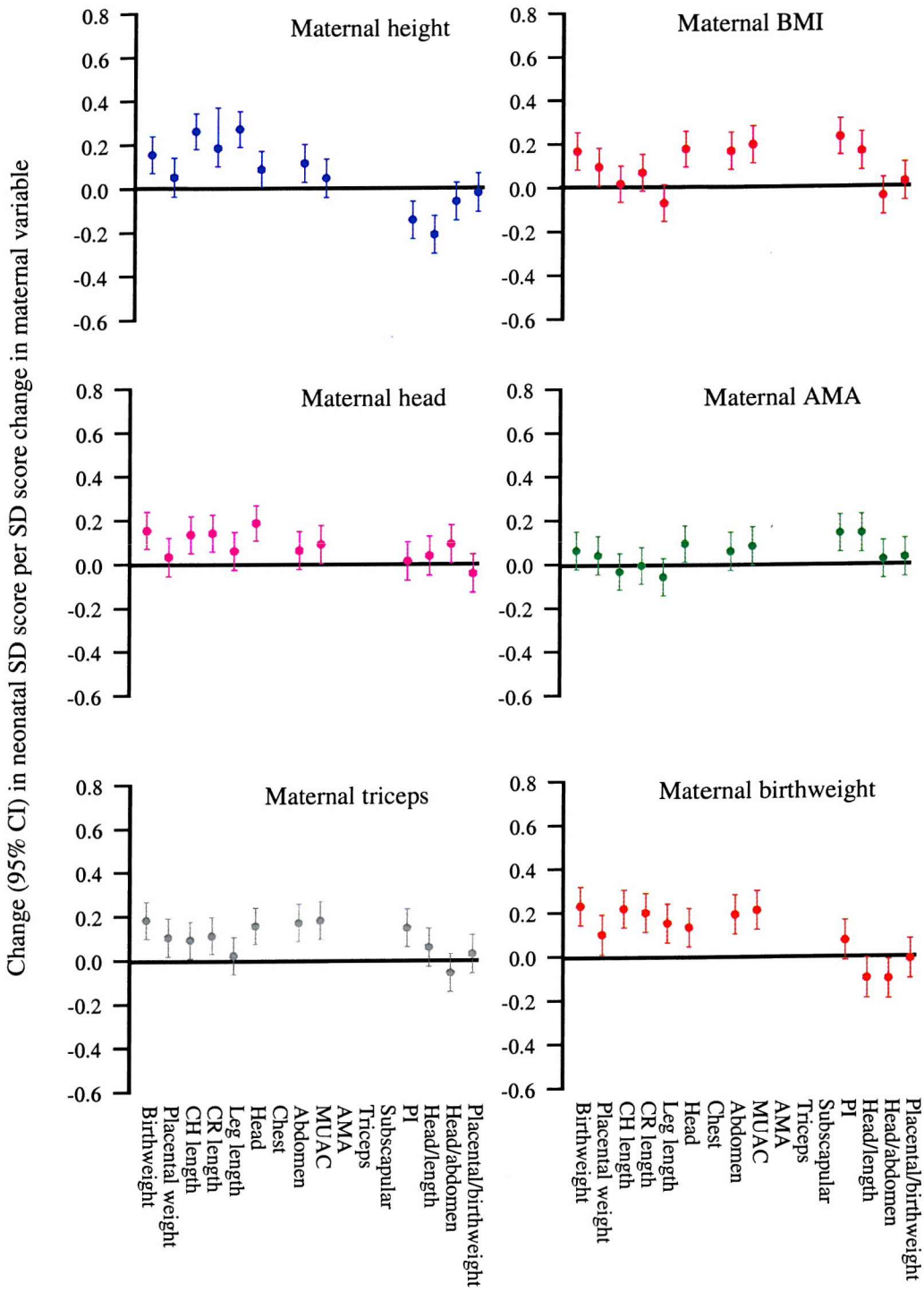
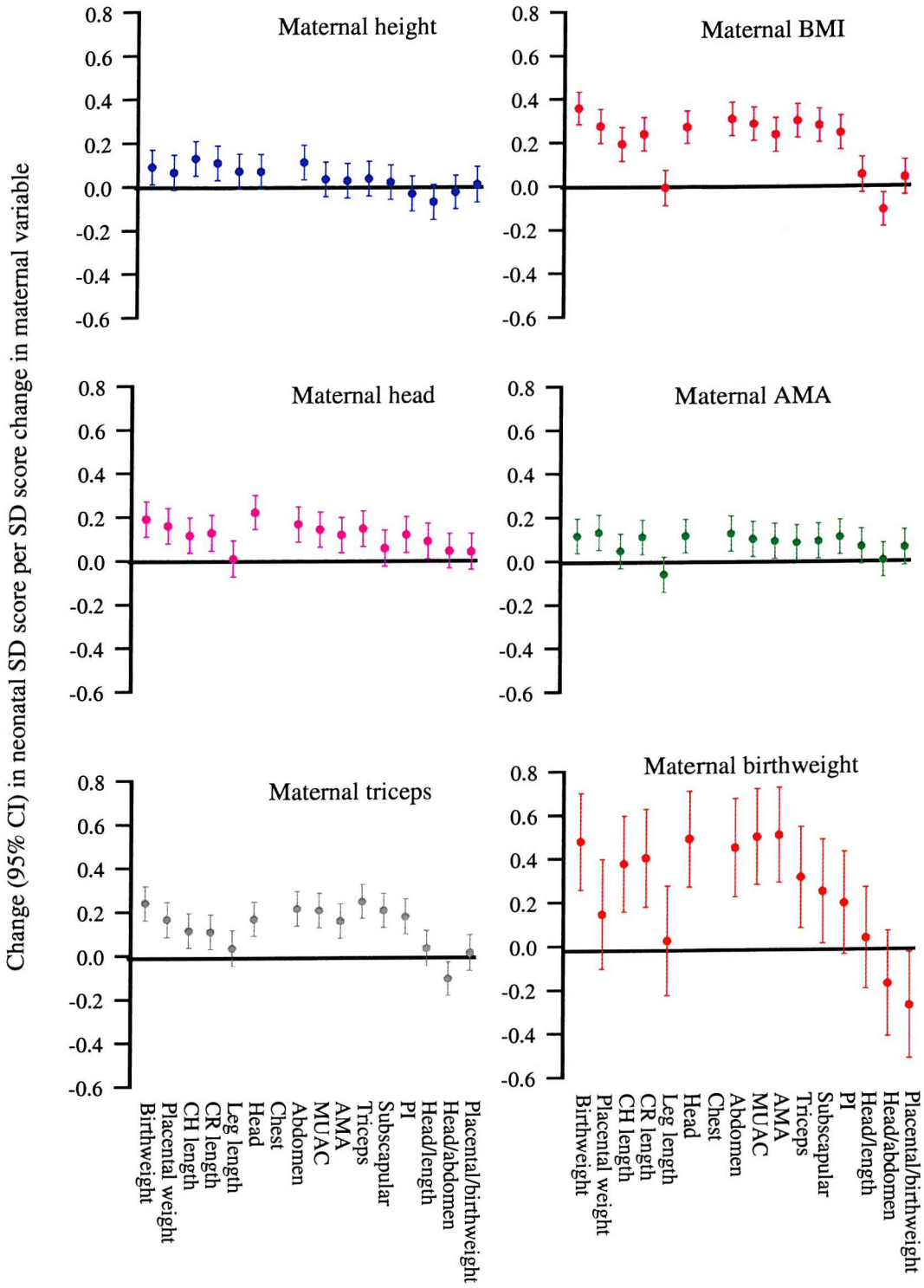


Figure 6.14b Effects of maternal variables on neonatal variables – Mysore 2



6.3.3 Comparison across maternal measurements

The effects of the different maternal measurements on each neonatal measure were compared within each dataset. Sets of maternal variables outlined at the start of §5.3 were used for this analysis. A series of graphs was constructed to illustrate the effect of an increase the size of the IQR of the maternal measure, on the neonatal variable. For example, if maternal height was increased by the size of the IQR that ranged from approximately 7 to 10cms across the datasets (see Table 6.2), then the increases expected in each of the neonatal variables are shown. IQRs were used, as comparable measures between maternal variables that had originally been measured in different units were required. As maternal BMI, AMA and triceps skinfold had skewed distributions, IQRs were used in preference to SDs.

Table 6.2 IQRs for maternal variables

	Height (cm)	BMI (kg/m^2)	Head (cm)	AMA (cm)	Triceps (mm)	Maternal birthweight (g)
Pooled data						
Set 1	10.4	4.7				
Set 2	9.9		2.8	8.6	11.5	
Set 3	9.8			8.7	10.5	
Set 4	10.5		2.5	11.0	11.0	737
Individual data						
Southampton 1	8.0	5.3				
Southampton 2	7.5	5.7	2.0	9.2	6.3	716
Southampton 3	10.0	5.6				
Southampton 4	8.0	5.4				
Farnborough	8.9	3.6				
Isle of Man	8.1	4.2				
Aberdeen	7.6	3.4				
Mysore 1	8.0	3.6				
Mysore 2	7.0	4.9	2.1	5.9	12.2	510
Pune 1	7.0	2.3	1.9	5.7	4.2	
Kandy, Sri Lanka	8.0	3.6				
Beijing	6.8	3.2				
Kasaji, Congo	7.8	3.1		6.6	4.9	
Imesi, Nigeria	7.6	2.3				
Kingston 1	8.3	6.1				
Kingston 2	8.0	4.5		10.9	5.6	

Graphs were drawn for each combination of maternal and neonatal measures. On each graph, pooled estimates of mean effect size with 95% confidence intervals are shown, which were obtained by including indicator variables for each dataset. Pooled IQR values

were different for each set of maternal variables, as they were dependent on which datasets were included. Other estimates with confidence intervals were derived from separate datasets. All effects were adjusted for neonatal sex and gestation. Again, linearity was assumed for simplicity. Both individual and simultaneous effects of the maternal variables were of interest. Datasets were restricted to mother-baby pairs where the mother had complete data for the all the variables in the model of interest to allow fair comparisons between individual and simultaneous effects.

All the maternal body components had important effects on the neonatal measures. In general, after adjustment for other maternal variables in each model, the effects remained similar, as shown in Figures 6.15a and b for neonatal birthweight.

Figure 6.15a **Individual maternal height, head, AMA and triceps effects on neonatal birthweight**

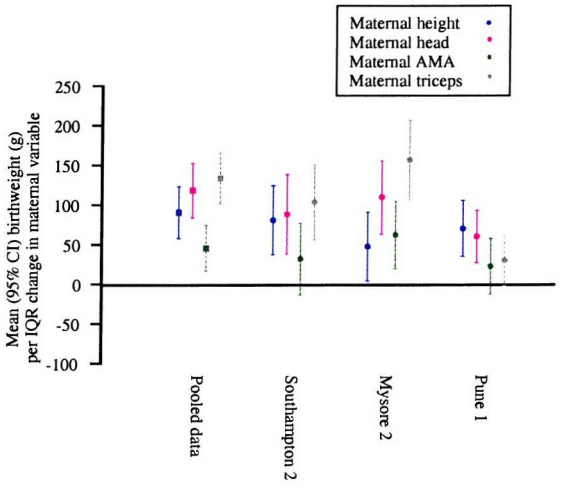
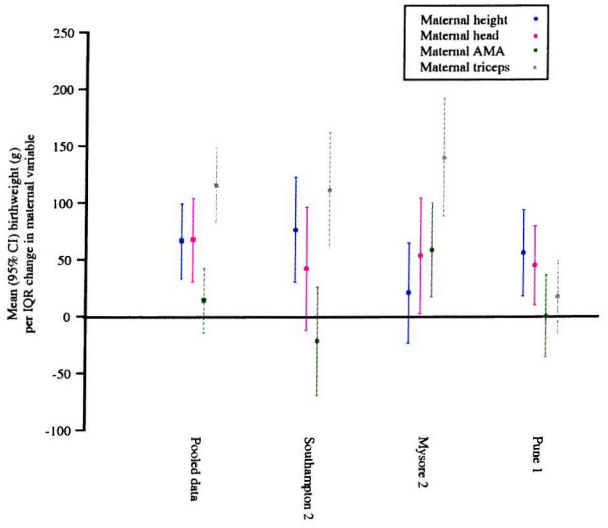


Figure 6.15b **Simultaneous maternal height, head, AMA and triceps effects on neonatal birthweight**

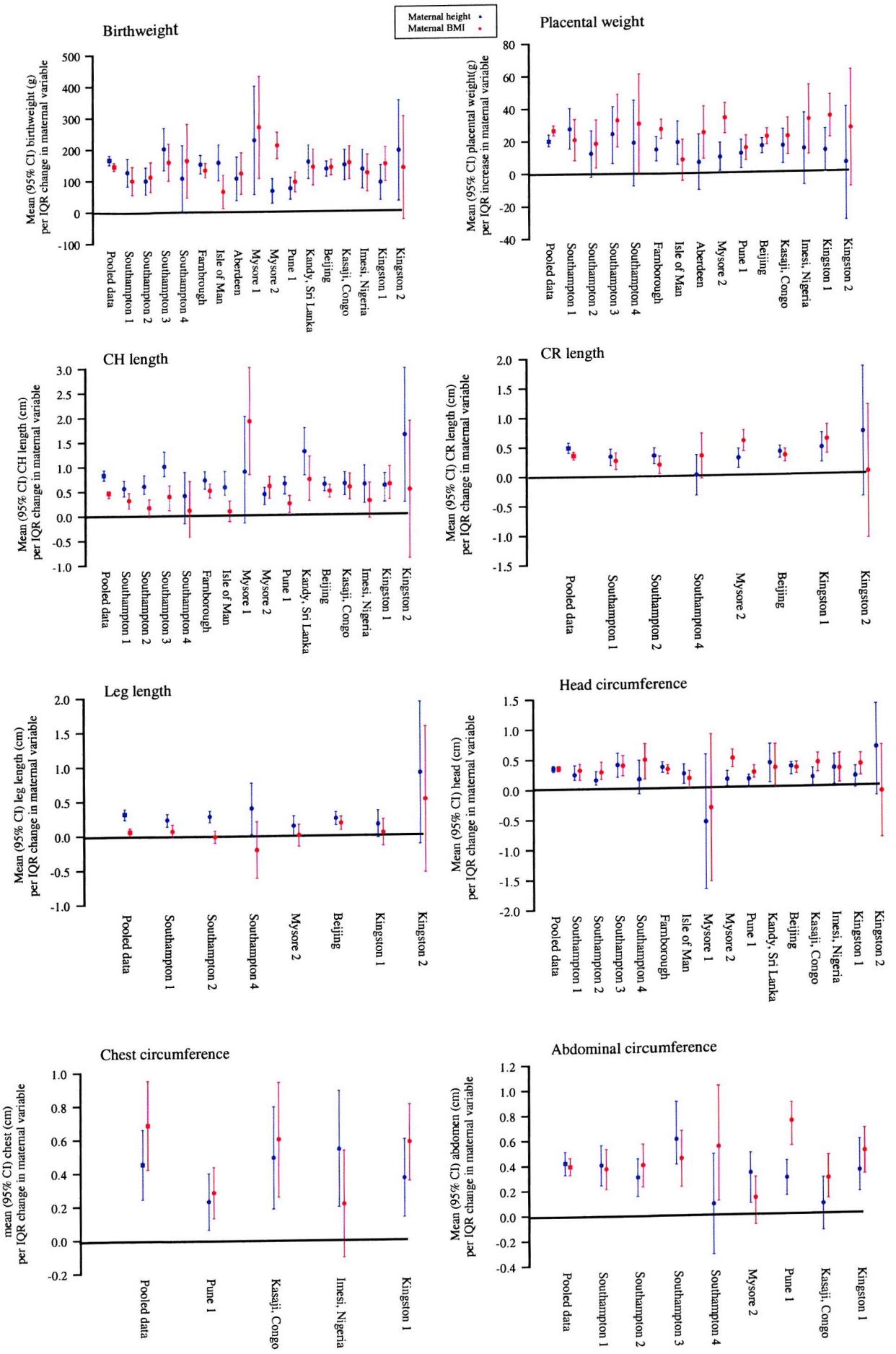


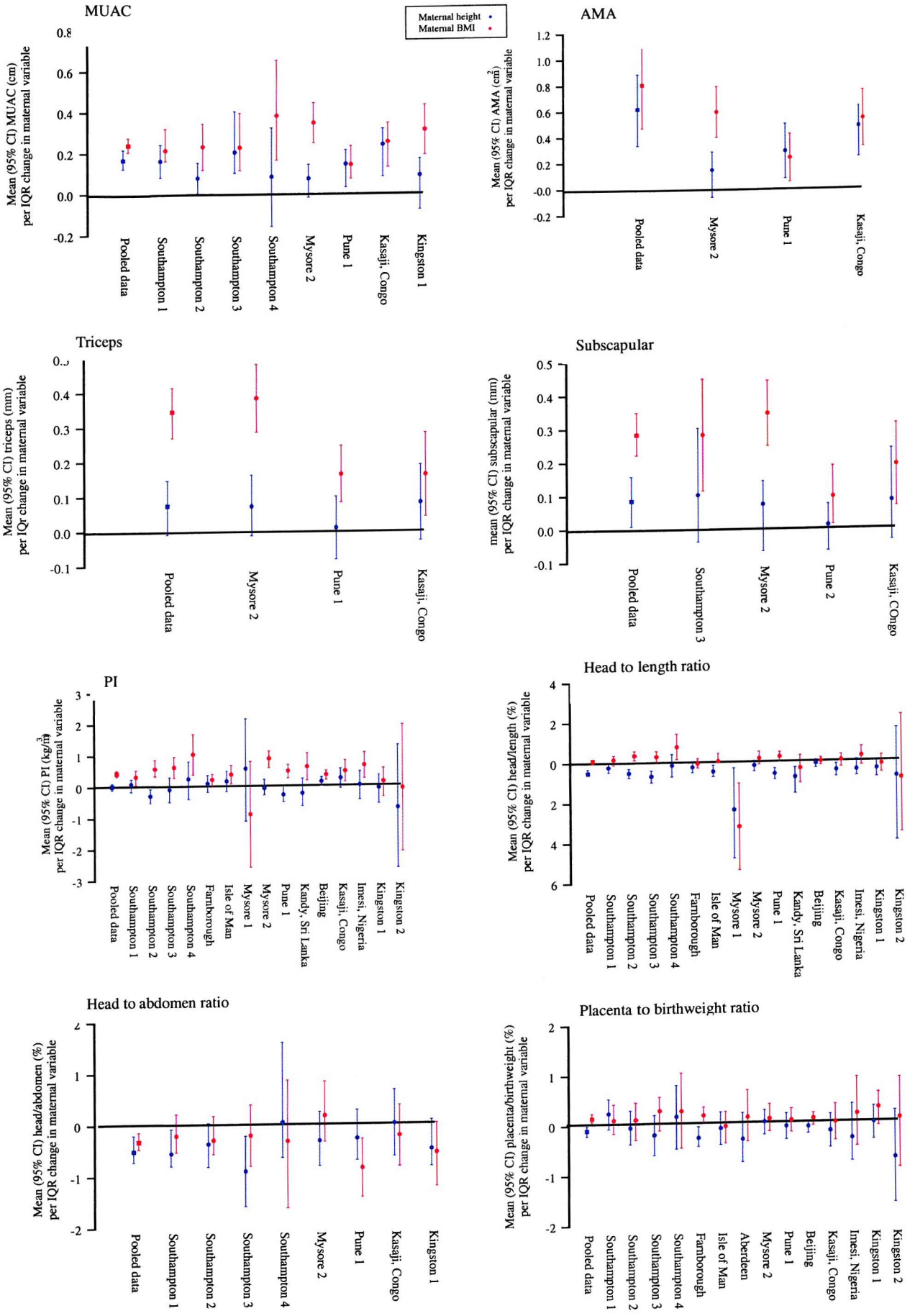
The only exception was maternal head circumference which became considerably less important unless relationships were in Pune 1, or were with neonatal head circumference. All of the following results therefore refer to the simultaneous effects of the maternal variables.

Maternal height and BMI

Figure 6.16 shows the simultaneous effects of maternal height and BMI on each of the neonatal variables.

Figure 6.16 Maternal height and BMI effects on neonatal variables



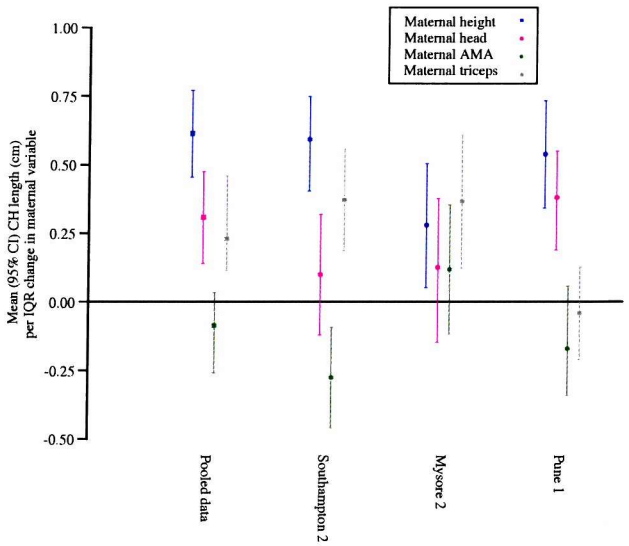

MUAC
Maternal height
Maternal BMI
Mean (95% CI) MUAC (cm) per IQR change in maternal variable
Pooled data
Southampton 1
Southampton 2
Southampton 3
Southampton 4
Mysore 2
Pune 1
Kasaji, Congo
Kingston 1
AMA
Mean (95% CI) AMA (cm²) per IQR change in maternal variable
Pooled data
Mysore 2
Pune 1
Kasaji, Congo
Triceps
Mean (95% CI) triceps (mm) per IQr change in maternal variable
Pooled data
Mysore 2
Pune 1
Kasaji, Congo
Subscapular
mean (95% CI) subscapular (mm) per IQR change in maternal variable
Pooled data
Southampton 3
Mysore 2
Pune 2
Kasaji, COngo
PI
Mean (95% CI) PI (kg/m²) per IQR change in maternal variable
Pooled data
Southampton 1
Southampton 2
Southampton 3
Southampton 4
Farnborough
Isle of Man
Mysore 1
Mysore 2
Pune 1
Kandy, Sri Lanka
Beijing
Kasaji, Congo
Imesi, Nigeria
Kingston 1
Kingston 2
Head to length ratio
Mean (95% CI) head/length (%) per IQR change in maternal variable
Pooled data
Southampton 1
Southampton 2
Southampton 3
Southampton 4
Farnborough
Isle of Man
Mysore 1
Mysore 2
Pune 1
Kandy, Sri Lanka
Beijing
Kasaji, Congo
Imesi, Nigeria
Kingston 1
Kingston 2
Head to abdomen ratio
Mean (95% CI) head/abdomen (%) per IQR change in maternal variable
Pooled data
Southampton 1
Southampton 2
Southampton 3
Southampton 4
Mysore 2
Pune 1
Kasaji, Congo
Kingston 1
Placenta to birthweight ratio
Mean (95% CI) placenta/birthweight (%) per IQR change in maternal variable
Pooled data
Southampton 1
Southampton 2
Southampton 3
Southampton 4
Farnborough
Isle of Man
Aberdeen
Mysore 2
Pune 1
Beijing
Kasaji, Congo
Imesi, Nigeria
Kingston 1
Kingston 2

Maternal height was generally a stronger predictor of the neonatal lengths than maternal BMI. Maternal BMI had a stronger effect than maternal height on placental weight, neonatal MUAC, skinfolds and PI. Otherwise the effect of these two maternal variables was similar. For example the effect of maternal height and BMI on neonatal birthweight were surprisingly similar except in Mysore 2, where maternal BMI was much more important.

Maternal height, head, AMA and triceps

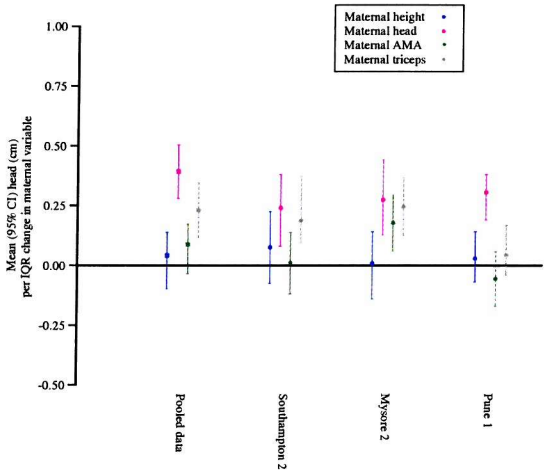
Of these maternal measurements, height was the strongest predictor of the neonatal length variables. Figure 6.17 compares the effects on CH length.

Figure 6.17 Maternal height, head, AMA and triceps effects on CH length



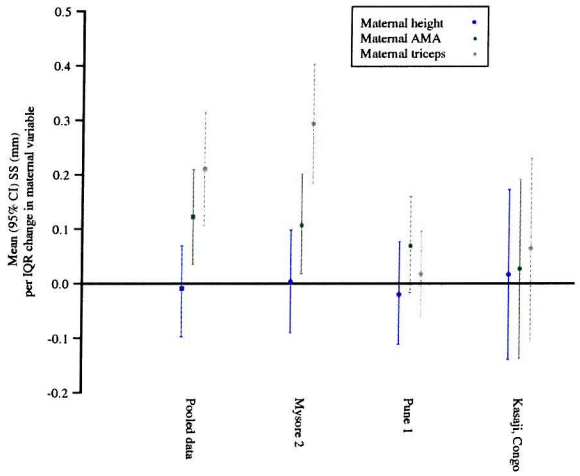
Maternal head circumference was the strongest predictor of neonatal head circumference (Figure 6.18).

Figure 6.18 Maternal height, head, AMA and triceps effects on neonatal head circumference



Maternal tricep skinfold was the strongest predictor of the neonatal fat measures (Figure 6.19) except in Pune 1 where maternal head circumference had the strongest effect.

Figure 6.19 Maternal height, AMA and triceps effects on neonatal subscapular



These 'like with like' relationships were not seen with muscle. Maternal triceps skinfold in Southampton 2 and Mysore 2, head circumference in Pune and AMA in Kasaji were the strongest predictors of neonatal MUAC (Figure 6.20) and AMA (Figure 6.21).

Figure 6.20 Maternal height, head, AMA and triceps effects on neonatal MUAC

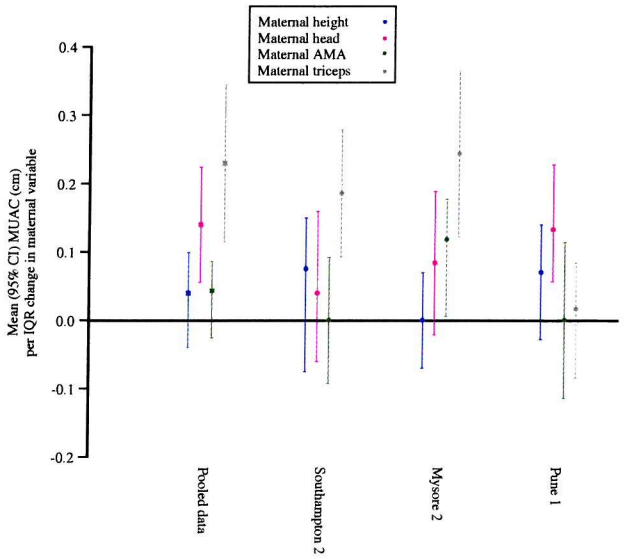
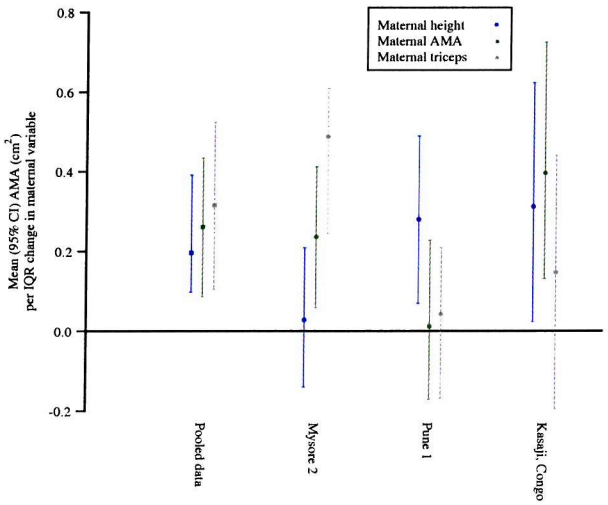
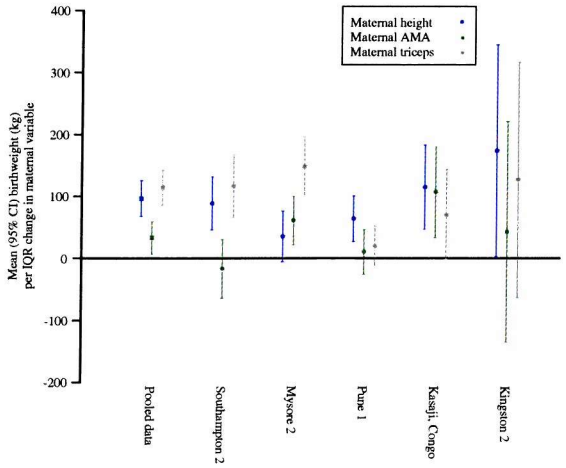


Figure 6.21 Maternal height, AMA and triceps effects on neonatal AMA



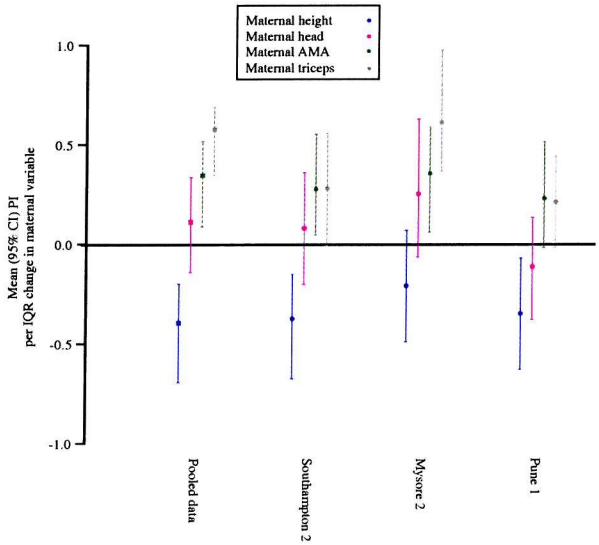
When comparing the effects of maternal AMA and triceps across all the neonatal measures, triceps tended to have a stronger effect than AMA, particularly in Mysore 2. However, the opposite was true in Kasaji, with the triceps having a weaker effect than AMA. Figure 6.22 shows the relationships with neonatal birthweight.

Figure 6.22 Maternal height, AMA and triceps effects on neonatal birthweight



The pattern of relative effect size of the maternal variables varied across the datasets in general. However the pattern for PI was remarkably similar (Figure 6.23), suggesting that thin babies were born to tall, thin mothers.

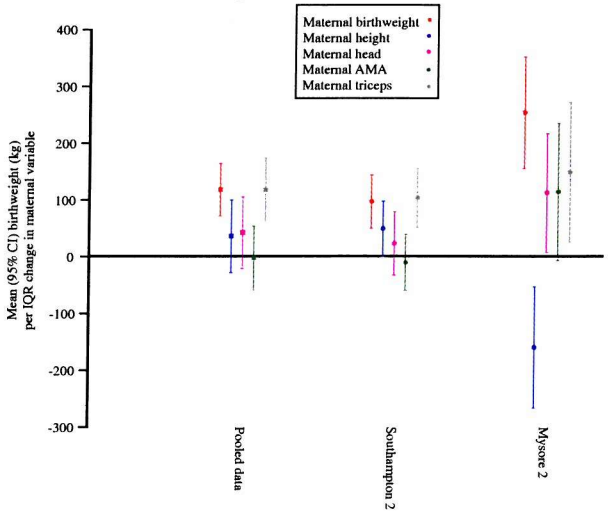
Figure 6.23 Maternal height, head, AMA and triceps effects on PI



Maternal birthweight

When maternal birthweight was considered in addition to the adult variables, it was the strongest predictor of all of the neonatal measurements in Mysore 2. In Southampton 2, either maternal birthweight or triceps skinfold were the strongest predictors of most of the neonatal measurements, although the 'like with like' relationships remained for maternal height and neonatal length, and also maternal head and neonatal head. Figure 6.24 shows the effects of all the maternal variables on neonatal birthweight.

Figure 6.24 Maternal birthweight, height, head, AMA and triceps effects on neonatal birthweight



Interactions between maternal measurements were also examined, using the four sets of maternal variables. There were very few which were significant, and in these cases significance was only weak, and likely to have been obtained by chance due to the large number of tests that were undertaken.

6.4 Comparison of neonates with similar mothers

The extent that geographical differences in neonatal phenotypes were explained by differences in their mother's phenotype were investigated using two approaches.

6.4.1 Adjustment for maternal phenotype

Individual maternal variables each accounted for up to 15% of the variation in neonatal measures within datasets, with the exception of maternal birthweight where the value was higher. Up to 25% of the variation was explained by the combinations of maternal variables, and again, this value was higher if maternal birthweight was included.

The effects of the dataset locations on each of the neonatal measurements, before and after adjusting for four sets of maternal variables were investigated. 'Constrained' linear regression was used, where each model constant was constrained to be equal to the overall mean neonatal value. This enabled comparisons to be made between the regression estimate for each dataset location and the overall mean, rather than an arbitrarily chosen regression estimate for one of the dataset locations. The overall mean for each neonatal

outcome was calculated using all datasets combined, and the same value was used in each of the four sets of maternal variables for comparability.

The neonatal outcomes were adjusted for gestation before analysis, and neonatal sex was included in the models. Indicator variables for each dataset were also included. Maternal variables were categorised and combined before they were used as adjusters. This overcame difficulties, although shown to be minor, with non-linear relationships between maternal and neonatal variables, and interactions between maternal variables. The same combinations of maternal variables were used as explained at the start of §5.3:

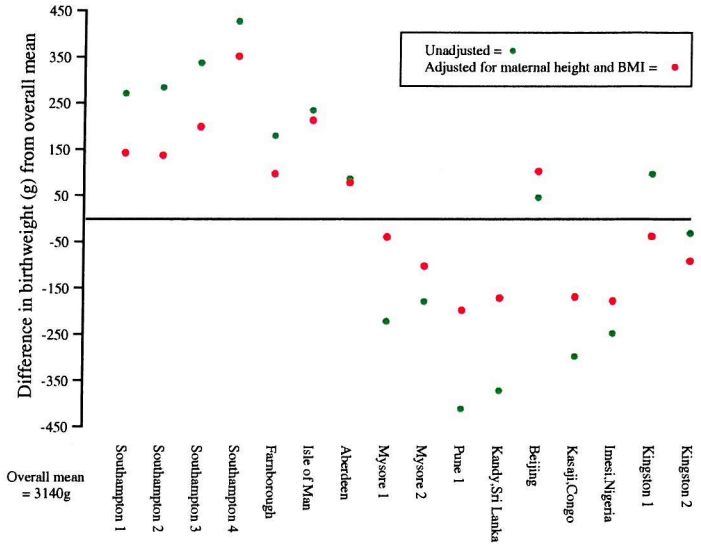
- Maternal height and BMI – four groups each then combined
- Maternal height, head, muscle, fat – two groups each then combined
- Maternal height, muscle, fat – three groups each then combined
- Maternal height, head, muscle, fat, birthweight – two groups each then combined.

Maternal variables and also neonatal sex were centred to allow calculation of true dataset location effects after constraining the model constant to equal the mean neonatal value. Datasets were restricted to mother-baby pairs where the mother had complete data for all the variables in the model of interest to allow fair comparisons between unadjusted and adjusted dataset location effects.

Maternal height and BMI

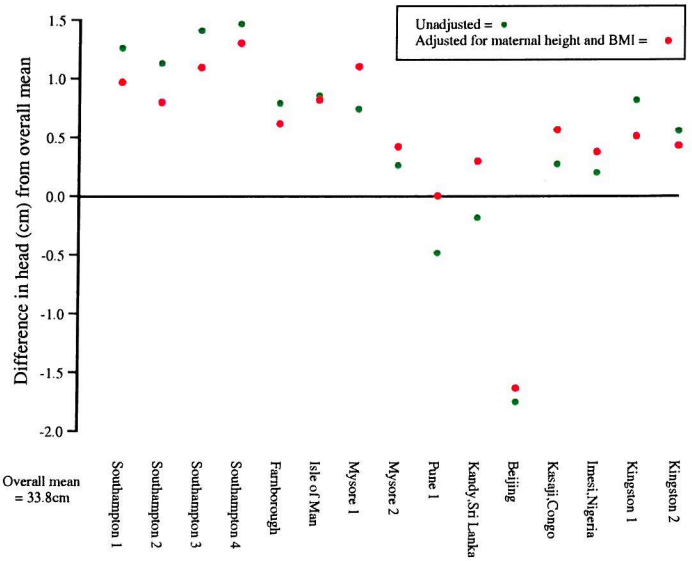
Before adjustment, neonates in the UK were generally larger and those in India, Sri Lanka and Africa generally smaller than the overall means for neonatal birthweight, placental weight, length and the circumferences (green dots in Figure 6.25 for birthweight). After adjusting for maternal height and BMI, these differences were substantially reduced, although still remained (red dots in Figure 6.25).

Figure 6.25 Maternal height and BMI and neonatal birthweight



In China and Jamaica, neonates were similar to the overall mean level before adjustment, and there were no substantial changes after adjustment. The only exception was head circumference in Beijing, which was substantially reduced before adjustment, and was not affected to a great extent by adjustment (Figure 6.26).

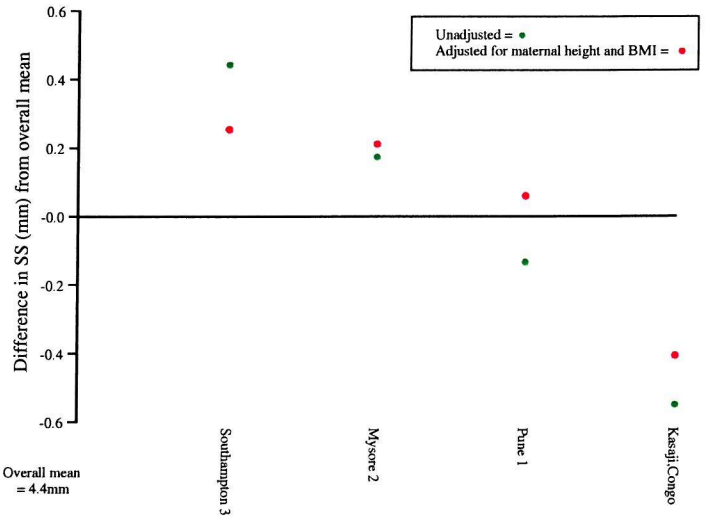
Figure 6.26 Maternal height and BMI and neonatal head circumference



Changes after adjustment for the maternal variables were generally most marked in Pune 1, and Kandy. The smallest changes tended to be in China and Africa.

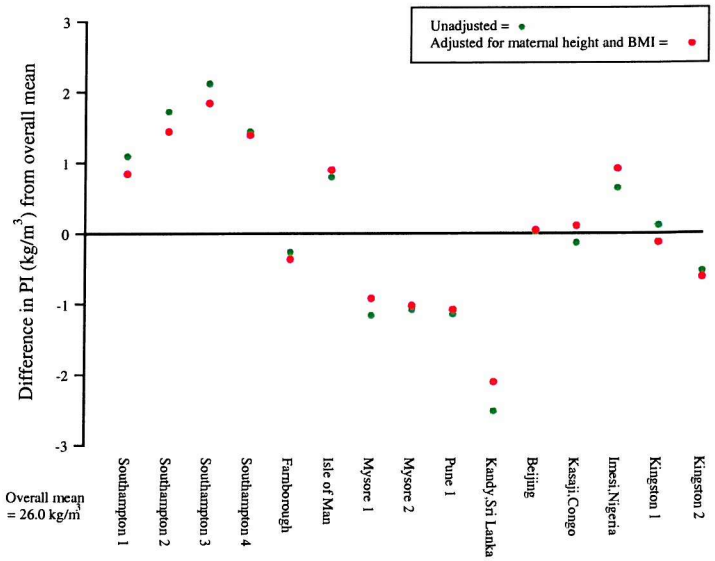
For AMA and skinfolds, neonates in Southampton and Mysore 2 had larger values and Pune 1 had smaller values than the overall means. These were generally reduced, after adjustment for the maternal variables. Neonates also had smaller values in Kasaji, and these did not change substantially after adjustment for the maternal variables. Figure 6.27 shows the patterns for the subscapular skinfold.

Figure 6.27 Maternal height and BMI and neonatal subscapular skinfold



Changes in PI and the other ratio variables after adjustment for the maternal variables were very small (Figure 6.28).

Figure 6.28 Maternal height and BMI and neonatal PI



Other maternal measures

Adjustment for maternal variables other than height and BMI generally made less difference to the effect size (Figure 6.29, 6.30 and 6.31 for neonatal birthweight, MUAC and subscapular skinfold respectively), particularly for the model including maternal birthweight. Hence, maternal height and BMI explained differences in birth size as well as individual components such as muscle and fat. Effects may not be visible if there is little difference in size between unadjusted and adjusted values.

Figure 6.29 Four sets of maternal variables and neonatal birthweight

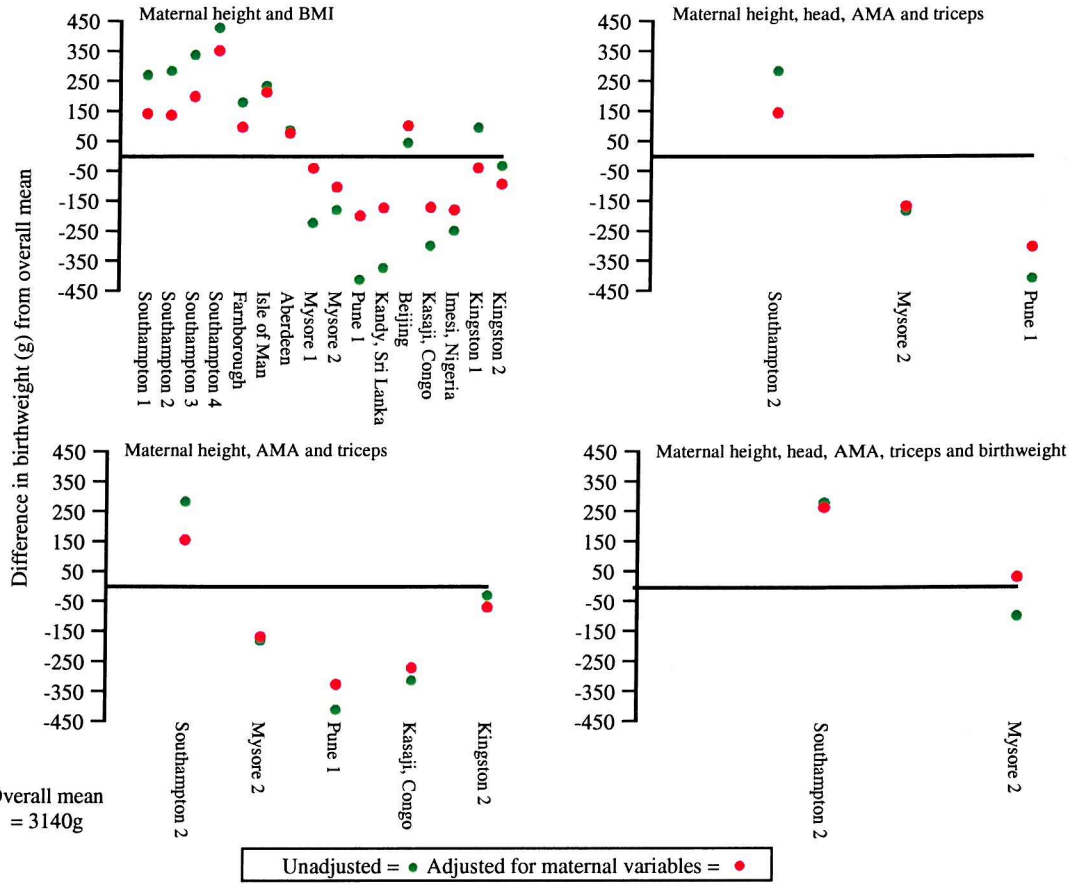


Figure 6.30 Four sets of maternal variables and neonatal MUAC

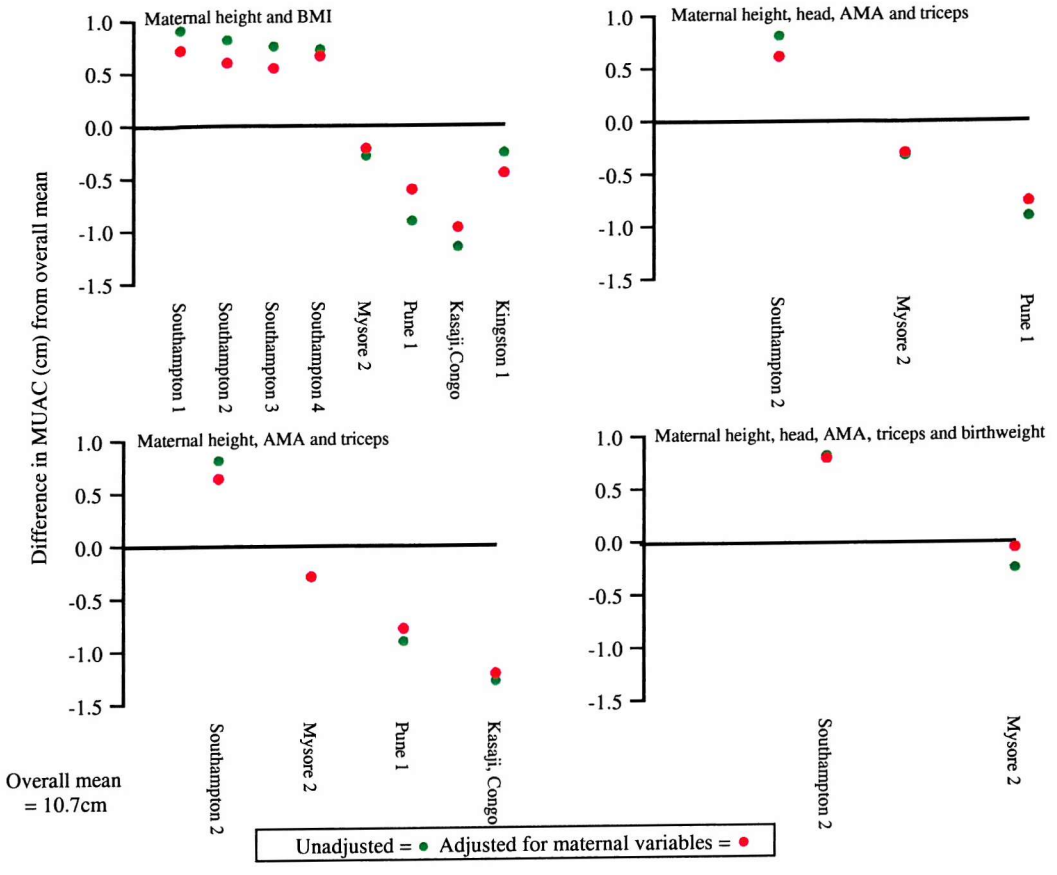
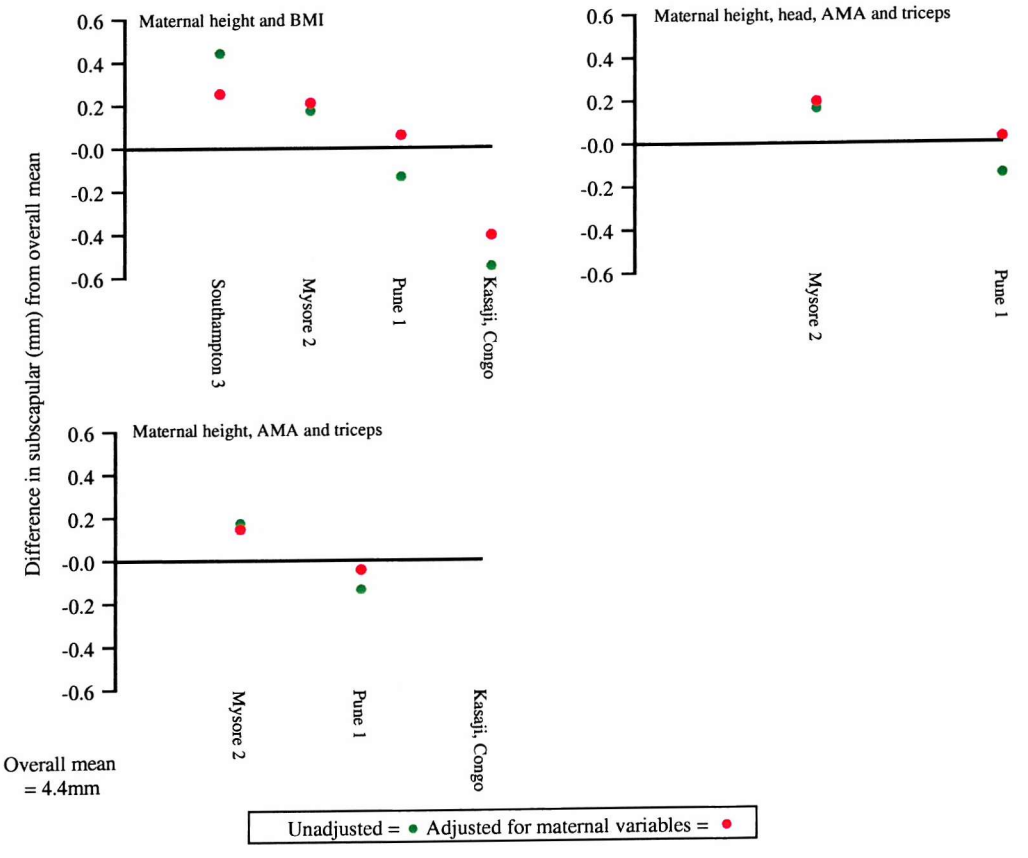


Figure 6.31 Four sets of maternal variables and neonatal subscapular



6.4.2 Comparison within maternal phenotypes

Neonates with similar mothers were compared across datasets. Regression was used to predict the neonatal outcomes for mothers with different phenotypes. Three stages of analysis were required:

- Selection of maternal phenotypes
- Derivation of prediction models
- Prediction of neonatal outcomes.

Maternal variables were restricted to height and BMI to enable most datasets to be included in the analysis.

Selection of maternal phenotypes

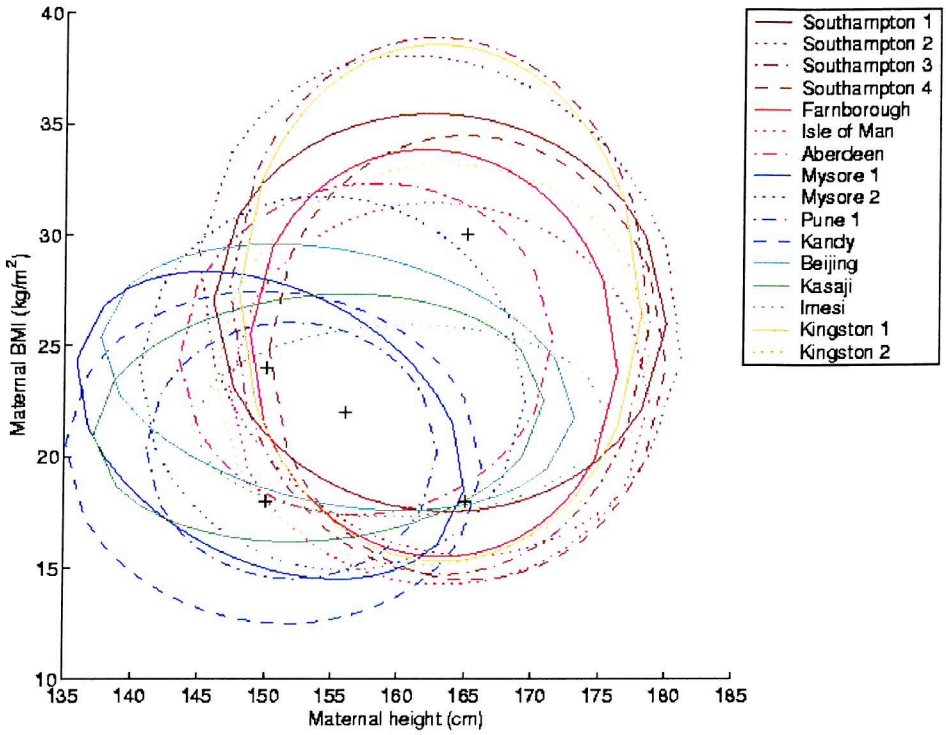
For each dataset, an ellipse was constructed that encompassed 95% of the mothers, based on height and BMI. The restriction to 95% of the data was imposed so as to include mothers that were representative of the population. Details of the method for deriving the ellipses are shown in Appendix 4d. Figure 6.32 displays the ellipses for each of the datasets.

The ellipses were used to select values for the different maternal phenotypes, which are shown in Table 6.3. The aim was to include extremes of the distributions while also including as many datasets as possible. As there were no mothers with very high BMI in the datasets where there were very short mothers, BMI values were chosen to be different for short and tall mothers. These phenotypes are marked with crosses in Figure 6.32. The 'standard mother' was based on the central point of the area covered by all of the superimposed ellipses to include all datasets.

Table 6.3 Maternal phenotypes

Phenotype	Height (cm)	BMI (kg/m^2)
Standard	156	22
Short, thin	150	18
Short, fat	150	24
Tall, thin	165	18
Tall, fat	165	30

Figure 6.32 Maternal height and BMI distributions



Indian, Sri Lankan, Chinese and African women had relatively small BMI ranges as illustrated by ellipses with smaller vertical than horizontal axes. Ranges for maternal height were similar sizes. The position of the ellipses indicated the size of the mothers. Those in Europe and Jamaica (top right) were tall and fat, those in India and Sri Lanka (bottom left) were short and thin, and those in China and Africa (bottom) were thin but their heights varied.

Derivation of prediction models

The second step was to derive regression equations to use for predicting neonatal outcomes from maternal height and BMI simultaneously. F tests were used to assess whether full quadratic models fitted the data significantly better than linear models for each outcome in each of the datasets. For consistency, these were only based on mothers that were included inside the ellipses. Appendix 4e shows the forms of prediction models that were selected. In most cases, linear models were adequate.

Regression coefficients were obtained from the appropriate models, again based only on mothers inside the ellipses. Neonatal outcomes were adjusted for gestational duration where possible. Contour plots were constructed for each neonatal outcome in each dataset, with the contour lines corresponding to different values of the neonatal outcome.

For example, Figure 6.33a and b show the contour plots for neonatal birthweight (in grams) in Southampton 1 (linear) and Southampton 2 (quadratic) respectively. Contours were only plotted inside the ellipses to correspond with maternal height and BMI combinations that were feasible for the relevant population.

Figure 6.33a Contour plot for neonatal birthweight in Southampton 1

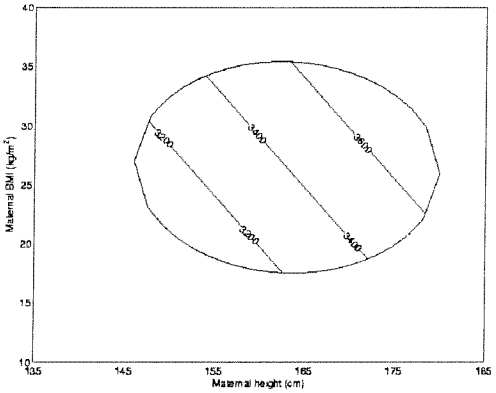
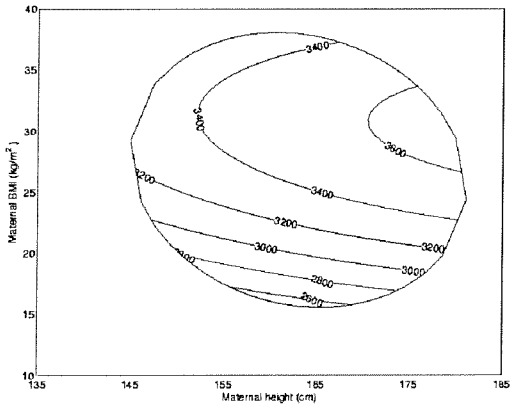


Figure 6.33b Contour plot for neonatal birthweight in Southampton 2



Prediction of neonatal outcomes

For each of the five maternal phenotypes, neonatal outcome values were predicted in each of the datasets using the regression coefficients described above. Values were only predicted if mothers with the relevant phenotypes existed in the dataset.

When the actual mean values were compared with those predicted for a 'standard mother' who was 156cm tall with a BMI of 22kg/m^3, variation was reduced to some extent, although patterns across datasets remained similar. Figure 6.34 shows this comparison for

neonatal birthweight, along with all the predicted birthweights across the datasets for the other four maternal phenotypes.

Figure 6.34 Actual neonatal birthweights and predicted values for different maternal phenotypes

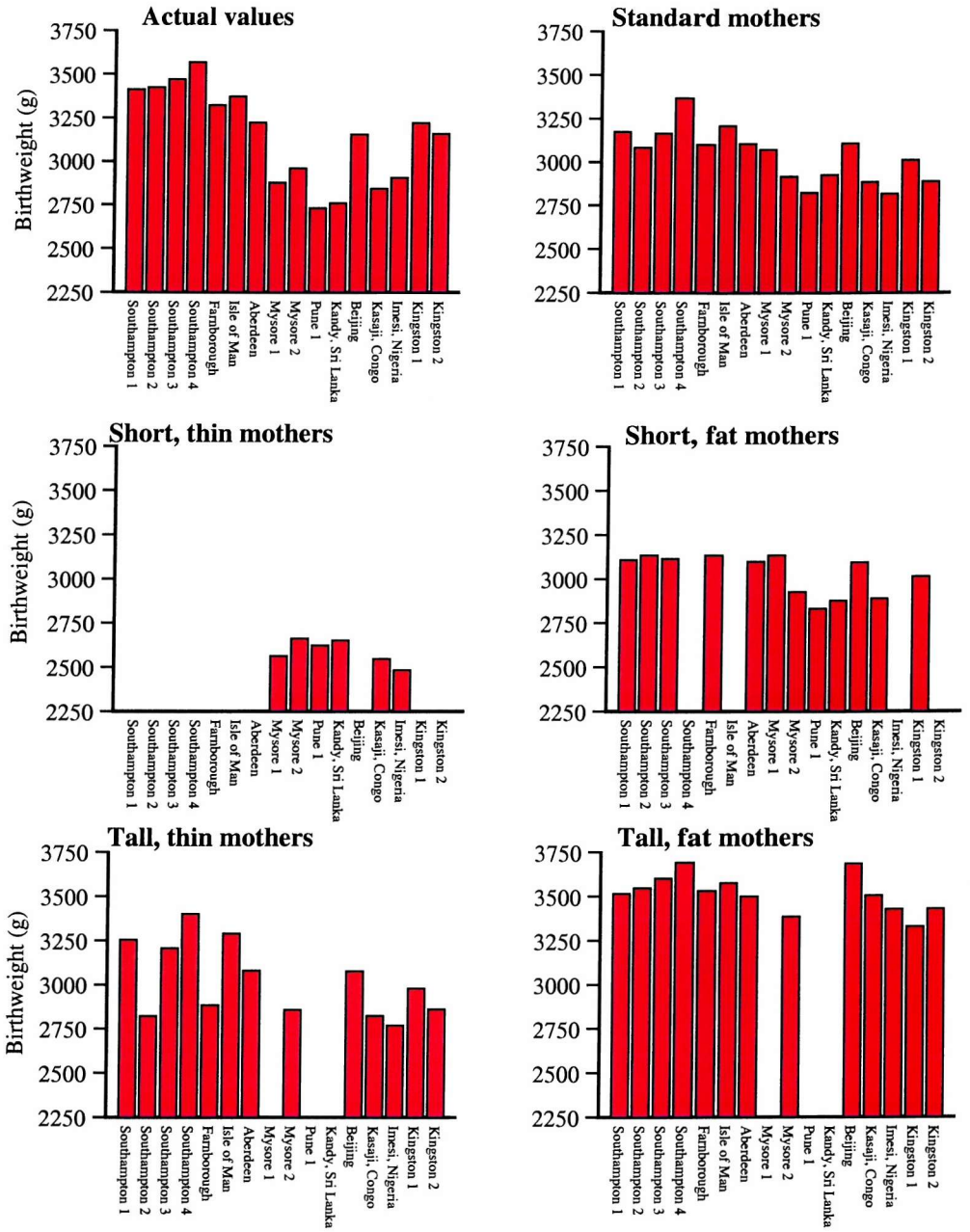


Table 6.4 shows the ranges in the predicted values for each of the four maternal phenotypes, plus the standard phenotype for comparison.

Table 6.4 Ranges in predicted values by maternal phenotype

Maternal phenotype Neonatal measure	Short, thin (N=6)	Short, fat (N=12)	Tall, thin (N=13)	Tall, fat (N=13)	Standard (N=16)	Actual (N=16)
Birthweight (g)	178	303	630	364	550	836
Placental weight (g)	37	148	136	152	144	199
CH length (cm)	2.1	2.6	3.3	2.3	2.9	2.9
CR length (cm)	-	1.4	1.5	2.1	1.7	1.8
Leg length (cm)	-	1.1	1.3	1.7	1.2	1.1
Head (cm)	2.1	2.7	3.1	2.3	3.0	3.2
Chest (cm)	3.2	2.5	3.5	2.3	2.9	3.4
Abdomen (cm)	1.6	2.6	1.6	1.9	3.9	4.5
MUAC(cm)	0.7	1.5	1.6	1.3	1.5	2.1
AMA (cm^2)	1.9	1.5	1.6	0.7	1.5	1.8
Triceps (mm)	0.2	0.5	0.3	0.9	0.5	0.5
Subscapular (mm)	0.6	0.6	0.6	0.9	0.6	1.0
PI (kg/m^3)	2.8	3.8	3.0	3.1	3.9	4.8
Head/length (%)	4.5	7.0	4.9	7.1	7.2	6.5
Head/abdomen (%)	5.8	7.4	2.9	10.6	9.5	9.5
Placenta/birthweight (%)	4.8	3.1	2.7	3.1	2.7	4.0

N = maximum number of datasets

When comparing the four maternal phenotypes, for most of the neonatal measurements, the differences between datasets were greatest for tall mothers. The predicted values for neonatal birthweight (Figure 6.34), CH length, head, chest and mid-upper arm circumference varied most for tall, thin mothers, while the values for placental weight (Figure 6.35), CR and leg length, the skinfolds and the ratio variables varied most for tall, fat mothers. However, the widest ranges for abdominal circumference and PI (Figure 6.36) were seen for short fat women, and the widest range for AMA (Figure 6.37) seen for short, thin women. It must be noted that short, thin women were only present in India, Sri Lanka and Africa, so smaller ranges would be expected, except for measurements that were only recorded in these datasets. Similar patterns were seen when the sexes were considered separately.

Figure 6.35 Actual neonatal placental weights and predicted values for different maternal phenotypes

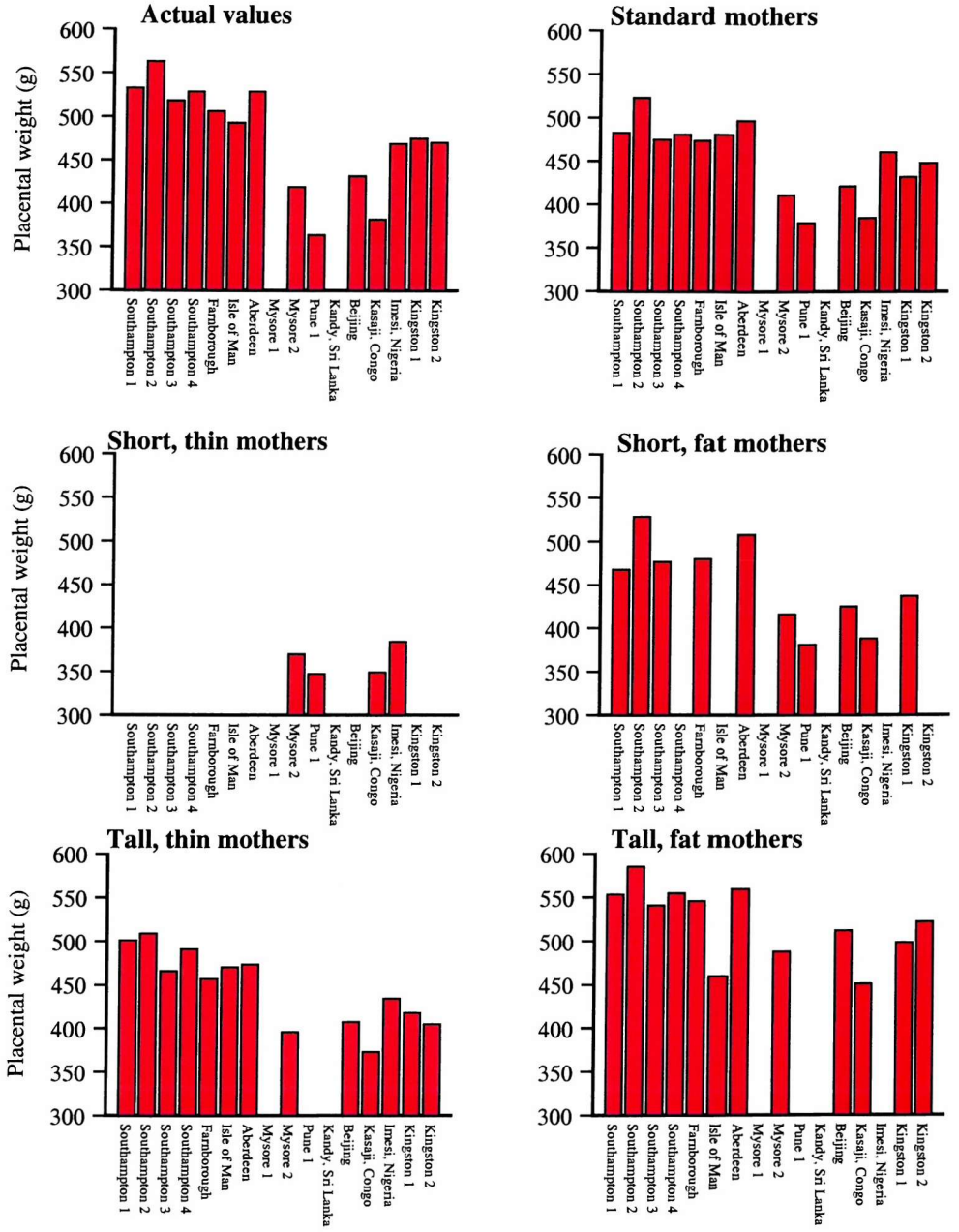


Figure 6.36 Actual neonatal PIs and predicted values for different maternal phenotypes

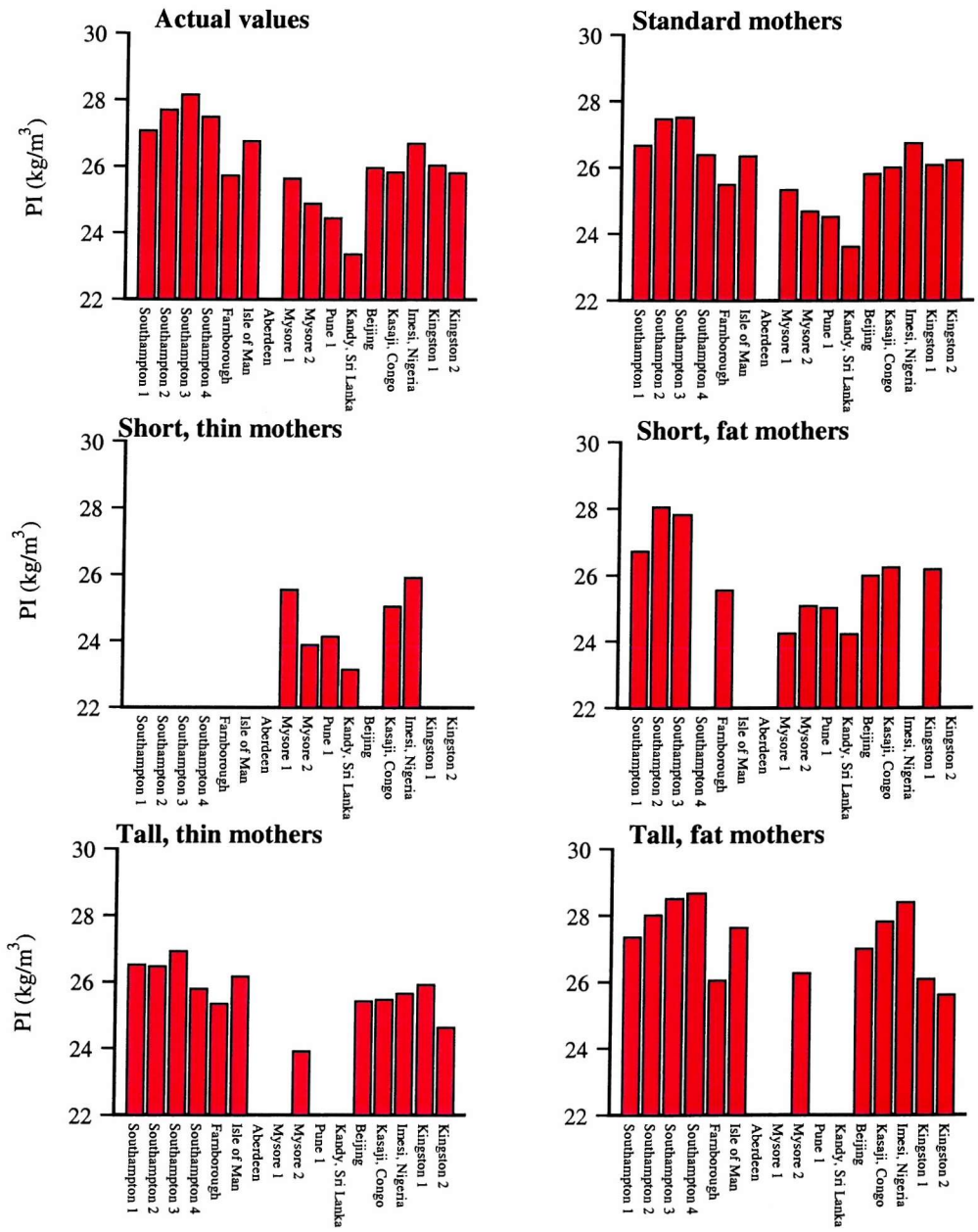
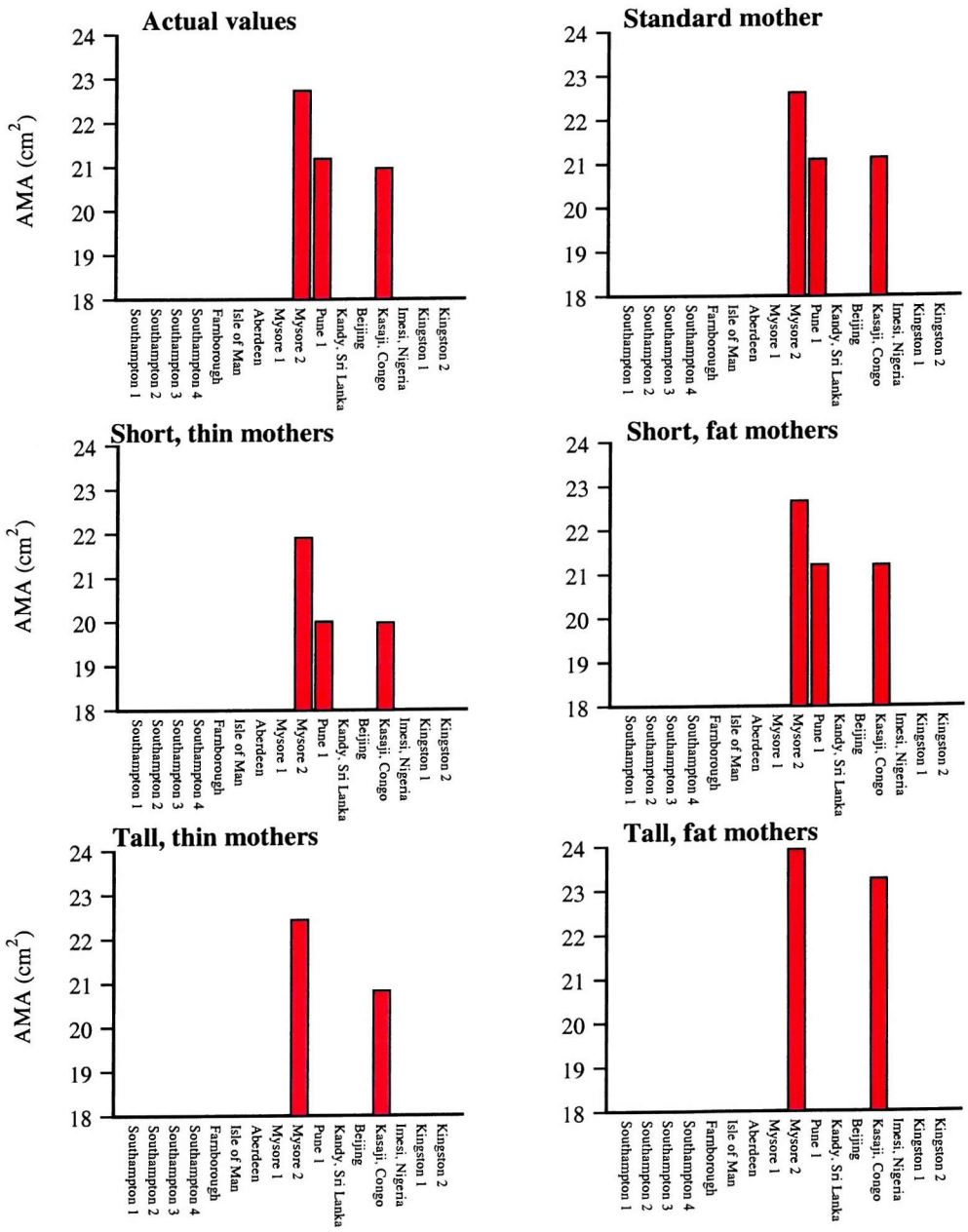


Figure 6.37 Actual neonatal AMAs and predicted values for different maternal phenotypes



6.5 Summary

Relationships between confounders:

- Maternal age and parity were highly positively correlated in all datasets.
- Older mothers and those of higher parity tended to have shorter pregnancies.
- There were no sex differences in maternal age, parity and gestation in most datasets.

Effects of confounders:

- In most datasets, older women with higher parities had higher BMI, AMA and triceps skinfolds, although effects of maternal age and parity were weakened if they were considered simultaneously. Older women, but those with lower parity were taller in some datasets, and these effects were strengthened after simultaneous adjustment. Maternal age and parity were not related to maternal head circumference.
- Maternal age, parity, and gestational duration had positive effects on all the direct neonatal measurements in most datasets, with the exception of parity and neonatal length. There were very few relationships with the neonatal ratio variables.

Comparison of mother to baby relationships:

- The maternal variables had positive effects on most of the neonatal measures, which were often similar across the datasets. However, there were stronger relationships with some of the neonatal measures for maternal height, BMI and birthweight in the developing countries, and for maternal AMA in Kasaji. Effects on the ratio variables were generally weaker.
- The only exception was in Kingston 2, where both maternal BMI and triceps skinfold had negative effects on CR length. This was in contrast to strong positive effects on leg length.
- For all the combinations of maternal and neonatal variables, separate intercepts were required for the different datasets.

Comparison of relationships across neonatal variables:

- All the maternal variables had relatively strong effects on neonatal birthweight. Strong effects were also seen for maternal height on neonatal length, for maternal BMI and head on neonatal head, and for maternal birthweight on neonatal muscle.
- Maternal height, head and birthweight had weak effects on placental weight, while maternal fat had weak effects on neonatal length.

Comparison of relationships across maternal variables:

- All the maternal variables had important effects on the neonatal measures. These were not weakened by adjustment for other maternal variables with the exception of head circumference.
- Within each dataset, the effects of maternal height and BMI were similar for many of the neonatal measures. However, BMI had a stronger effect than height on neonatal birthweight in Mysore 2.
- In general, 'like with like' relationships were seen for maternal height, head and fat. However, these relationships were not seen with muscle. Fat tended to have a stronger effect than muscle on the neonatal measures especially in Mysore 2, although the effects were reversed in Kasaji.
- Tall, thin mothers tended to have thinner babies, and this pattern was seen across the datasets.
- There was a strong effect of maternal birthweight on the neonatal measures, particularly in Mysore 2.

Comparison of neonates with similar mothers:

- Adjustment for maternal phenotype reduced differences considerably between populations, although they still remained.
- Knowledge of individual maternal components such as muscle and fat did not explain geographical differences any better than height and BMI alone.
- Changes after adjustment were generally more marked in India and Sri Lanka, and less marked in China and Africa.
- For mothers of the same height and BMI, neonates still varied across datasets, and for most measurements, particularly for taller mothers.

Therefore, mother to baby relationships were surprisingly similar across populations, although some maternal effects were stronger in developing countries. All the maternal variables had important effects on the neonatal measures, particularly maternal birthweight. 'Like with like' relationships were seen consistently for maternal height and neonatal length, and for maternal head and neonatal head. Maternal fat was also a strong predictor of neonatal fat amongst other measures, particularly in Mysore. Maternal muscle effects were relatively weak, except in Kasaji. The variation in maternal phenotypes across populations could explain differences in neonatal phenotypes to some extent.

7 Father to baby relationships

Firstly, the geographical differences in paternal phenotypes between and within countries were characterised. Then the effects of paternal measurements on neonatal phenotypes were analysed using some of the techniques from the mother to baby analyses. Finally comparisons were made between the effects of paternal and maternal measurements on neonatal phenotypes.

7.1 Characterisation of paternal phenotypes

Measurements were made on fathers in nine of the datasets in the main study. Height and weight were the only variables that were recorded in enough datasets to be of use. For the reasons outlined for the maternal measurements in §5.1, analysis was based on BMI rather than weight.

Each of the datasets in these analyses were restricted to father-baby pairs where father's height was recorded. Table 7.1 shows the numbers of father-baby pairs within each dataset that were used.

Table 7.1 Numbers used for analysis

Dataset	Number	% of original dataset excluded
Southampton 1	543	2.5%
Southampton 2	511	1.9%
Southampton 4	98	3.9%
Isle of Man	385	0.8%
Mysore 1	690	44.2%
Mysore 2	496	16.9%
Pune 1	599	5.4%
Kasaji, Congo	217	35.8%
Imesi, Nigeria	194	27.9%

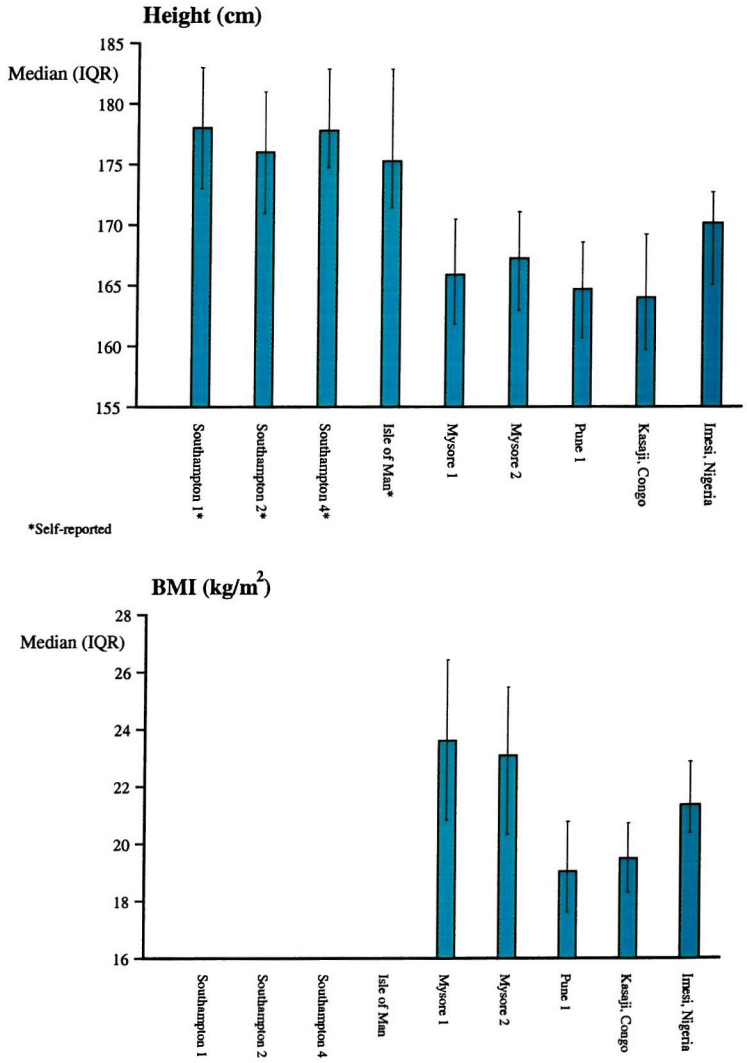
In Mysore 1, paternal data were only available if the child was born between 1957 and 1978 and followed up as a child or adult due to at least one of their parents being born in HMH hospital.

7.1.1 Size of fathers

Height was normally distributed in all datasets. BMI had a skewed distribution in each of the datasets in which it was recorded, so was dealt with appropriately in analyses.

Figure 7.1 shows the median values with IQRs for height and BMI in each dataset. A table of median values can be found in Appendix 5a.

Figure 7.1 Median (IQR) measurements



The tallest fathers were from the UK, although no measure of BMI was available in these datasets. Within India and Africa fathers from Mysore and Imesi (Nigeria) were the largest, with the fattest according to BMI from Mysore and the tallest from Imesi. The smallest fathers were from Pune and Kasaji (Congo), with the thinnest in Pune and the shortest in Kasaji. Hence BMI differences between the urban Mysore and rural Pune

populations were more marked, while height differences between the two rural African populations were more marked.

When comparing with maternal phenotypes, patterns were generally similar except in Kasaji where the mothers were taller and fatter than the fathers in relation to the other datasets, and hence the striking differences between the African datasets did not exist (see Figure 5.1).

7.1.2 Intercorrelations between measurements

Spearman correlation coefficients were calculated between height and BMI in each of the datasets. Results can be seen in Table 7.2, coloured according to size ($|r|<0.10$ $0.10\leq|r|\leq0.20$ $|r|>0.20$ $|r|$ = absolute correlation).

Table 7.2 Spearman correlation coefficients for paternal measures

	Mysore 1	Mysore 2	Pune 1	Kasaji, Congo	Imesi, Nigeria
Height/BMI	0.04	-0.02	-0.05	0.19	-0.19

Height and BMI were not correlated in India. In the two African datasets there were significant correlations, but in opposite directions ($p=0.005$ in Kasaji, $p=0.01$ in Imesi). This differed from results for the mothers (Table 5.8), where the variables were weakly positively correlated in both the African datasets, and strongly negatively correlated in Mysore 1.

7.1.3 Indices of adiposity

As there were significant correlations between height and BMI in the African datasets (Table 7.2), it was of interest to see whether BMI could be improved upon as a measure of adiposity, using the optimisation procedure explained in §4.3.3.

For each dataset, a power for height, k, was chosen such that

Correlation [(weight/height^k) and height] = 0.

Table 7.3 shows the optimal power for height in each dataset. Powers for the Benn Index (Benn 1971) were calculated for comparison.

Table 7.3 Optimal powers for weight to height ratio

	k	p (Benn index)
Mysore 1	2.1	2.1
Mysore 2	1.9	1.9
Pune 1	2.0	2.0
Kasaji, Congo	2.5	2.6
Imesi, Nigeria	1.4	1.4

For the Indian datasets, the k values were approximately two, the value used for BMI. The k values were all within 0.1 of those calculated for the Benn index. Values were generally higher than those calculated for the mothers except in Imesi (Table 5.10)

It was not possible to consider maximising correlations with fat as well as minimising correlations with height, as no skinfold measurements were available. As these alternative indices were not comparable across populations, and were almost identical to BMI in India and not that different from BMI in Africa, this traditional index continued to be used as a measure of adiposity for the fathers.

7.2 Paternal effects on neonatal phenotype

Firstly, linearity in father to baby relationships was assessed. To investigate geographical variation in father to baby relationships, two methods were used. Regression was used to compare each father-baby relationship across datasets. Also within each dataset, the effects of each paternal measurement across all neonatal measures were compared, again using regression. The extent that geographical differences in neonatal phenotypes were explained by differences in their father's phenotype was also examined, by comparing neonates after adjusting for differences in paternal size.

7.2.1 Linearity of father to baby relationships

Linearity of the relationships between both paternal height and BMI and each neonatal measurement was assessed using F tests (Appendix 5b). Adjustments were made for neonatal sex and gestation.

Paternal height was positively linearly related to neonatal birthweight, length and head circumference in most of the datasets. It was generally negatively related to PI and the head to length ratio. There were no other consistent relationships with the neonatal

variables. Paternal BMI was positively linearly related to all the direct neonatal measurements and PI in most of the datasets. It was generally unrelated to the ratio variables.

7.2.2 Geographical variation in father to baby relationships

Individual father to baby relationships

The individual effects of paternal height and BMI on neonatal measures were compared across the datasets. In a series of separate graphs for each paternal-neonatal pair, regression lines were plotted for each dataset. F tests were used to investigate whether the paternal-neonatal relationships in each dataset could be represented by a common slope. If this was the case, further F tests were used to see if a common intercept could also be used. Neonatal variables were adjusted for gestation before analysis where possible. This analysis assumed linearity between each paternal and neonatal combination for simplicity, which has been shown to be generally acceptable.

Table 7.4a shows whether each paternal-neonatal relationship could be represented by a common slope, with p-values colour coded according to significance. The number of datasets used for each analysis is shown in brackets. Table 74b shows the range of estimates if separate slopes were required, or the common slope estimate if there were no significant differences in slopes.

Table 7.4a Common slopes test for each paternal-neonatal pair of measurements

p≥0.1 p<0.1 p<0.05 p<0.01

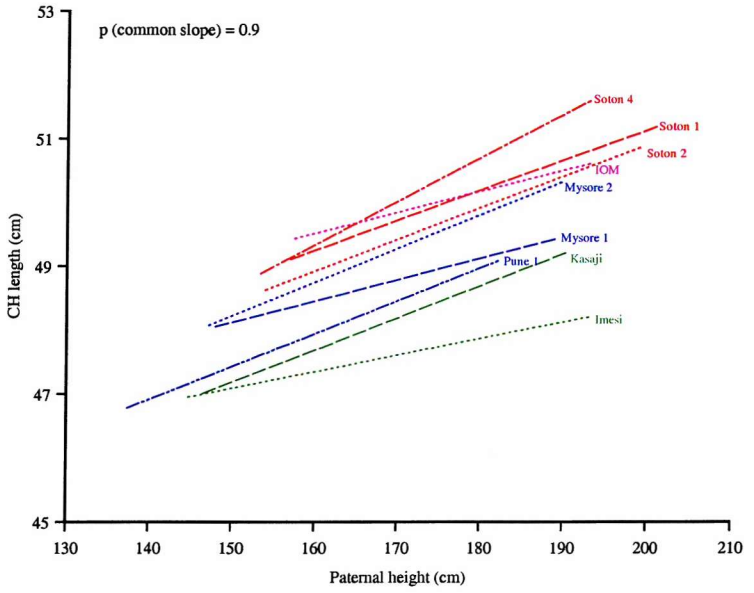
	Paternal variable P-value for common slope *(number of datasets)*	
Neonatal variable	Height	BMI
Birthweight	0.3*(9)*	0.02*(5)*
Placental weight	0.5*(9)*	0.1*(5)*
CH length	0.9*(9)*	0.04*(5)*
CR length	0.99*(4)*	*(0)*
Leg length	0.7*(4)*	*(0)*
Head	0.8*(9)*	0.05*(5)*
Chest	0.5*(3)*	0.03*(3)*
Abdomen	0.99*(6)*	0.8*(2)*
MUAC	0.2*(6)*	0.3*(3)*
AMA	0.2*(3)*	0.4*(3)*
Triceps	0.2*(3)*	0.8*(3)*
Subscapular	0.6*(3)*	0.3*(3)*
PI	0.01*(9)*	0.9*(5)*
Head/length	0.5*(9)*	0.2*(5)*
Head/abdomen	0.9*(6)*	0.9*(2)*
Placenta/birthweight	0.2*(9)*	0.5*(5)*

Table 7.4b Slope estimates for each paternal-neonatal pair of measurements

	Paternal variable Slope estimates	
Neonatal variable	Height (cm)	BMI (kg/m^2)
Birthweight (g)	6.73	-4.11 to 55.12
Placental weight (g)	0.62	2.42
CH length (cm)	0.04	-0.09 to 0.22
CR length (cm)	0.02	
Leg length (cm)	0.03	
Head (cm)	0.01	0.01 to 0.10
Chest (cm)	0.02	-0.04 to 0.22
Abdomen (cm)	0.02	0.07
MUAC (cm)	0.01	0.04
AMA (cm)	0.03	0.08
Triceps (mm)	0.003	0.03
Subscapular (mm)	0.002	0.03
PI (kg/m^3)		0.11
Head/length	-0.03	0.02
Head/abdomen	-0.01	-0.10
Placenta/birthweight	-0.01	-0.005

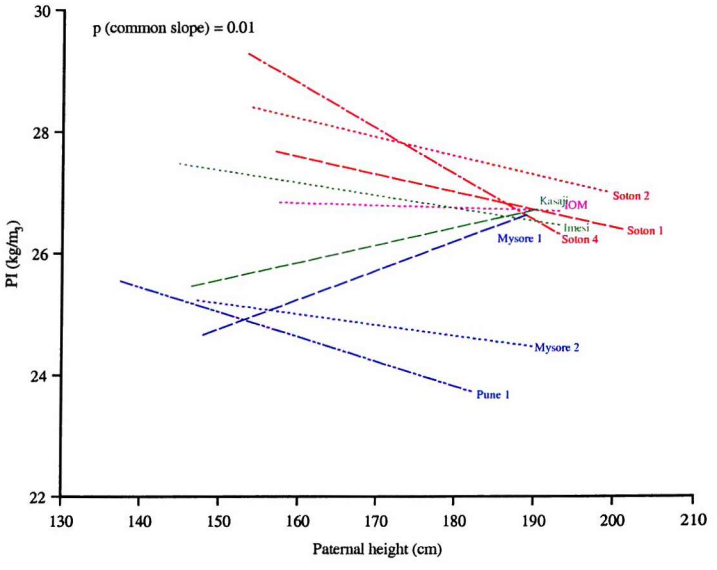
For almost all neonatal measures, common slopes could adequately represent relationships with paternal height. For example Figure 7.2 shows the relationship between paternal height and CH length, which was very similar across datasets.

Figure 7.2 Paternal height and CH length



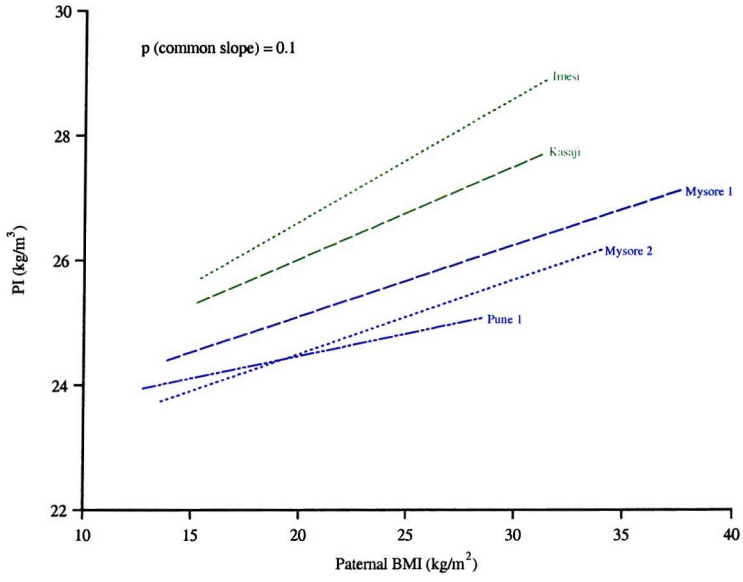
The only exception was the relationship with neonatal PI (Figure 7.3). In Mysore 1 and Kasaji paternal height and neonatal PI were positively related. However, in most datasets these variables were negatively related, although the strength of these relationships varied across the datasets. This could partly be explained by the relationships with neonatal CH length; in datasets where there were strong positive relationships with length, relationships with PI were strongly negative.

Figure 7.3 Paternal height and neonatal PI



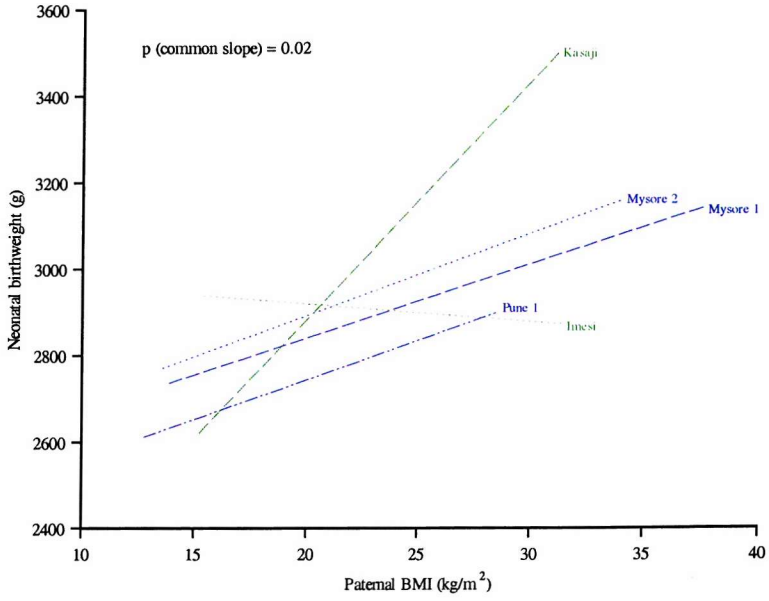
For paternal BMI, again most relationships with neonatal measures could be represented by a common slope for all datasets. Figure 7.4 shows the relationships with PI as an example.

Figure 7.4 Paternal BMI and neonatal PI



However, separate slopes were required for relationships between paternal BMI and neonatal birthweight, CH length and chest circumference. This was due to stronger positive relationships in Kasaji and negative but weaker relationships in Imesi. Figure 7.5 shows this for the relationship with neonatal birthweight.

Figure 7.5 Paternal BMI and neonatal birthweight



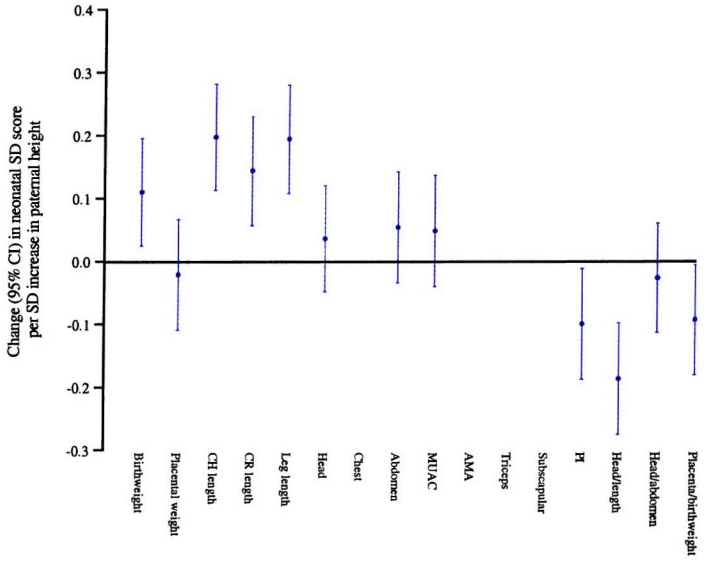
For all relationships between paternal and neonatal variables where a common slope was adequate, different intercepts were required for each dataset. In general, similar results were obtained if males and females were considered separately.

Comparison across neonatal measurements

The individual effects of paternal height and BMI on the different neonatal measures were compared within each dataset. The effect of an SD score increase in the paternal variable was illustrated as an SD score change in each neonatal measure, with adjustment for neonatal sex and gestation.

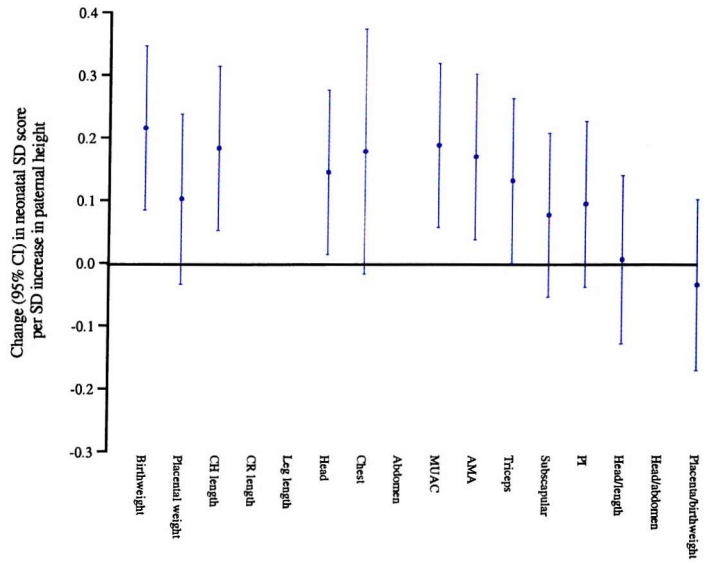
In most datasets, paternal height had strongest positive effects on neonatal length, particularly crown-heel and leg length. Relatively strong paternal height effects were also seen on the head to length ratio and to a lesser extent PI, although these were negative. This pattern is illustrated for Southampton 2 in Figure 7.6.

Figure 7.6 Effect of paternal height on neonatal variables – Southampton 2



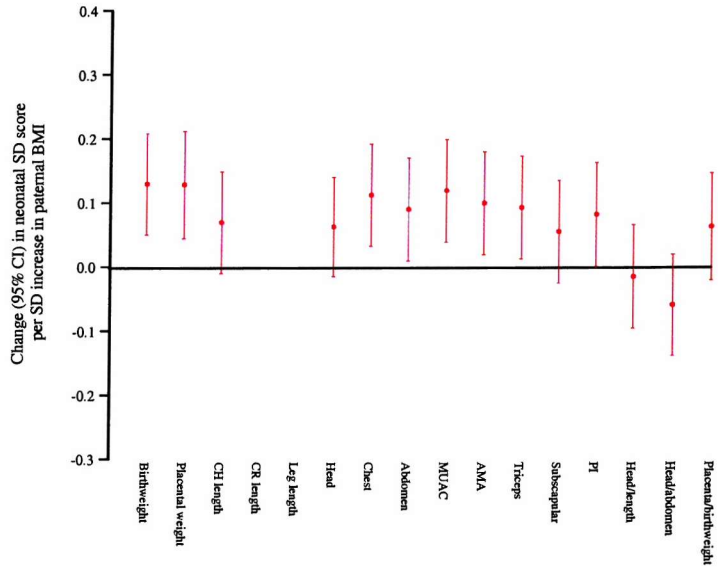
The only exception was in Kasaji, where paternal height had a similar positive effect across the direct neonatal measures, although had the strongest effect on birthweight (Figure 7.7).

Figure 7.7 Effect of paternal height on neonatal variables – Kasaji, Congo



The effect of paternal BMI was similar in magnitude across most of the neonatal measures, and Figure 7.8 shows this for Pune 1.

Figure 7.8 Effect of paternal BMI on neonatal variables – Pune 1



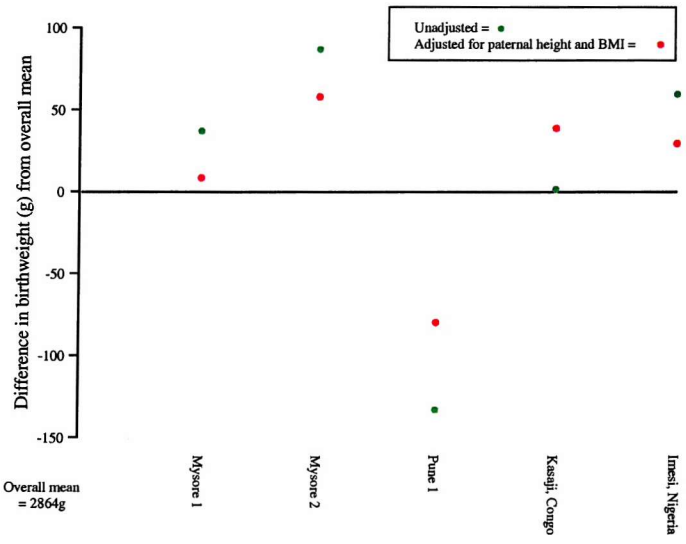
7.2.3 Comparison of neonates with similar fathers

Paternal variables accounted for up to 10% of the variation in neonatal measures within each dataset. Highest proportions were seen when paternal height predicted neonatal length. The effects of the dataset locations on each of the neonatal measures, before and

after adjusting for the paternal variables were investigated using the method described in §6.4.1.

Before adjustment, neonates in Mysore and Imesi were larger, while those in Pune and Kasaji were smaller than the overall means for most measures. Adjustment for paternal height and BMI reduced these differences, although they still remained. Figure 7.9 demonstrates the pattern for neonatal birthweight.

Figure 7.9 Paternal height and BMI and neonatal birthweight



7.3 Comparison of maternal and paternal effects on neonatal phenotype

Firstly, correlations between the maternal and paternal variables within each dataset were compared. The effects of maternal and paternal variables on the neonatal measures were then compared within each dataset, and finally adjustment was made for parental variables so that the effects of the dataset locations could be compared. Each analysis was undertaken twice; using height only so the UK datasets could be included, and then using both height and BMI which was only possible in India and Africa. Mysore 1 could not be used for the latter as only 10 neonates had data recorded for all parental variables. The BMI values at 30-weeks gestation were used for mothers as in previous analyses. Pre-pregnant values would have been preferable, but were only available in Pune.

7.3.1 Intercorrelations between maternal and paternal measurements

Spearman correlation coefficients were calculated between maternal and paternal height and BMI in each of the datasets where possible. Results can be seen in Table 7.5, coloured according to size ($|r|<0.10$ $0.10\leq|r|\leq0.20$ $|r|>0.20$ $|r|$ = absolute correlation).

Table 7.5 Spearman correlation coefficients for parental measures

	Maternal and paternal height	Maternal and paternal BMI
Southampton 1	0.08	
Southampton 2	0.12	
Southampton 4	0.03	
Isle of Man	0.29	
Mysore 1	0.22	
Mysore 2	0.28	0.24
Pune 1	0.18	0.14
Kasaji, Congo	0.27	0.15
Imesi, Nigeria	0.02	0.10

The parental heights were correlated in the Isle of Man, India and Kasaji. Parental BMIs were correlated in all datasets it was possible to use.

7.3.2 Comparison of maternal and paternal effects

The simultaneous effects of the parental variables on each neonatal measure were compared within each dataset. A series of graphs was constructed to illustrate the effect of an increase the size of the IQR in the parental measure on the neonatal variable, after adjusting for neonatal sex and gestation. Further details of this method were given in §6.3.3. Table 7.6 shows the IQRs for the parental variables. There are two sets of IQRs for the pooled data as those for height only included the UK datasets, while those for height and BMI were based on India (except Mysore 1) and Africa only.

Table 7.6 IQRs for parental variables

	Maternal height (cm)	Maternal BMI (kg/m^2)	Paternal height (cm)	Paternal BMI (kg/m^2)
Pooled data (height only)	10.6		12.3	
Pooled data (height/BMI)	7.8	3.5	8.6	4.4
Southampton 1	8.0		10.0	
Southampton 2	7.0		10.0	
Southampton 4	8.0		7.9	
Isle of Man	8.1		10.2	
Mysore 1	7.4		8.6	
Mysore 2	7.0	4.8	8.1	5.1
Pune 1	7.0	2.4	7.9	3.1
Kasaji, Congo	7.5	2.9	9.5	2.4
Imesi, Nigeria	5.1	2.2	7.6	2.3

Height

Maternal height had a stronger effect on the direct neonatal measures than paternal height in most datasets when considered simultaneously. For example, Figure 7.10 shows the comparison for neonatal birthweight, and Figure 7.11 for CH length.

Figure 7.10 Maternal and paternal height effects on neonatal birthweight

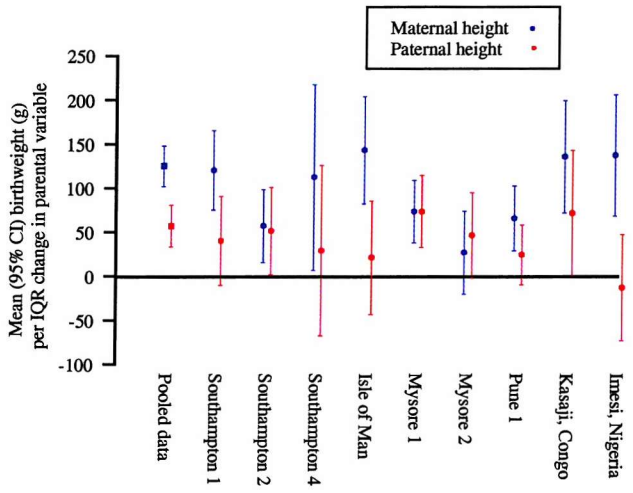
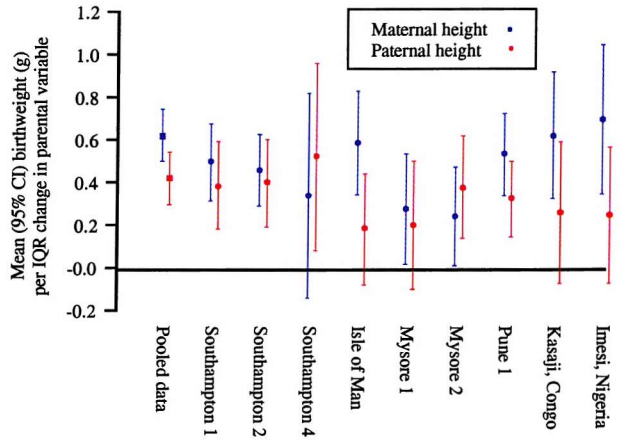


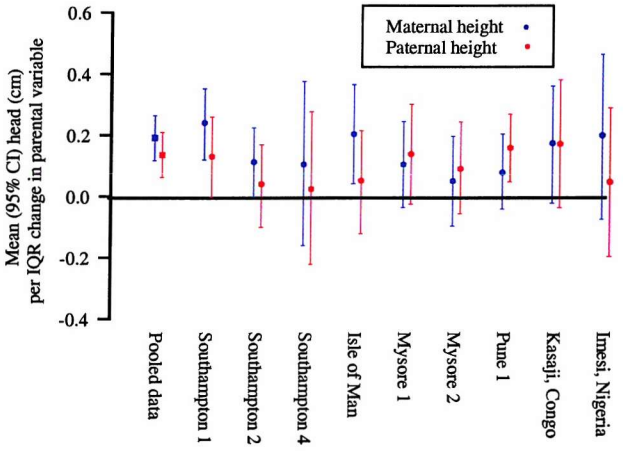
Figure 7.11 Maternal and paternal height effects on CH length



However in Mysore 2, paternal height had a stronger effect than maternal height on all neonatal measurements except CR length, abdominal circumference and the skinfolds (see Figure 7.10 for birthweight, Figure 7.11 for CH length).

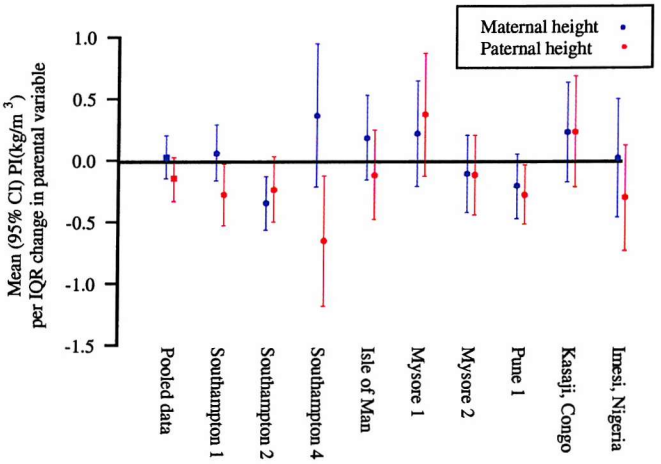
In addition, paternal height had a stronger effect than maternal height on neonatal head and abdominal circumference, AMA and skinfolds in Pune 1. Figure 7.12 shows the comparison for head circumference.

Figure 7.12 Maternal and paternal height effects on neonatal head circumference



For PI and the ratio variables the patterns were less consistent. For example paternal height had a stronger effect than maternal height on neonatal PI in many of the datasets (Figure 7.13).

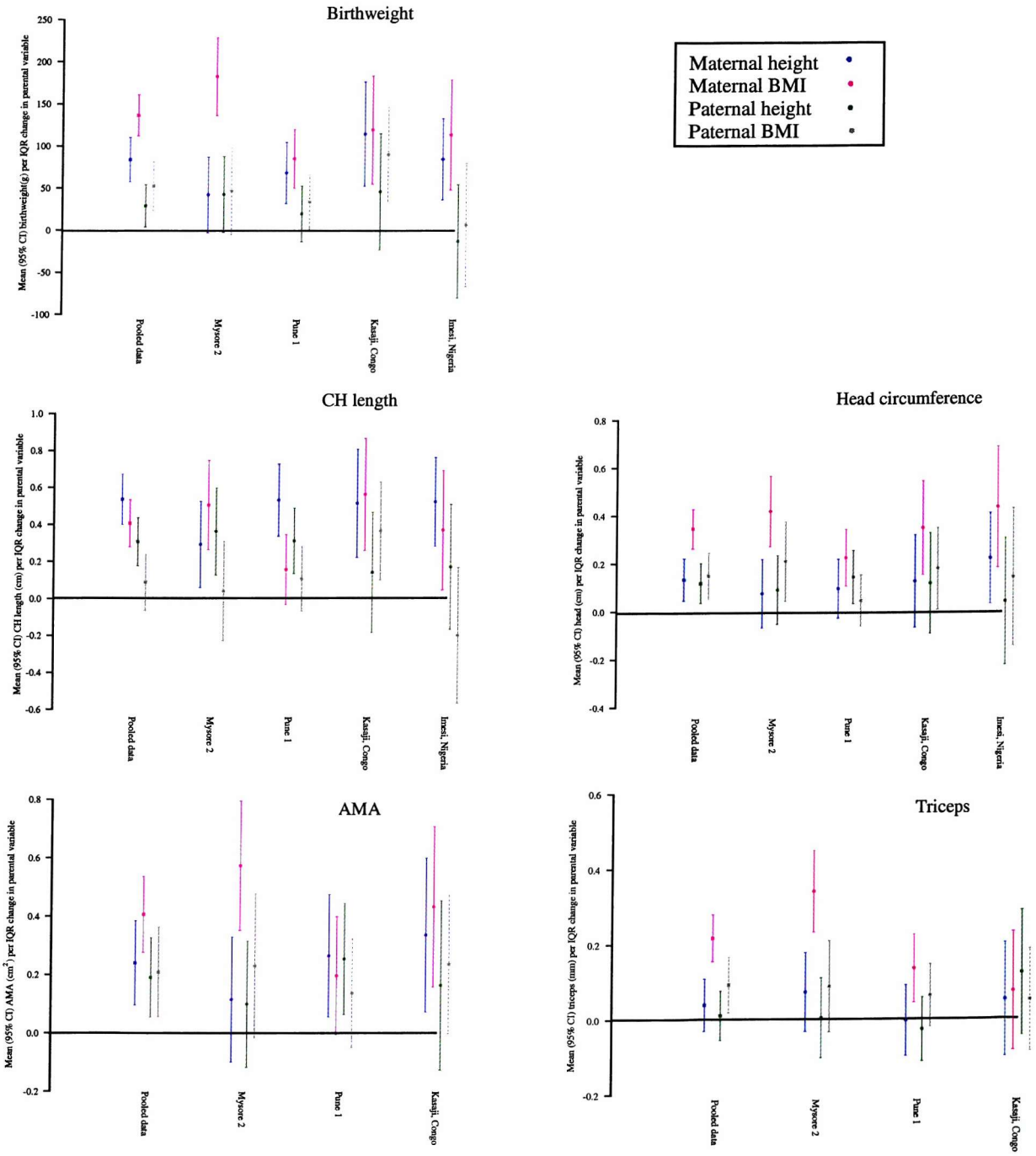
Figure 7.13 Maternal and paternal height effects on neonatal PI



Height and BMI

Considering simultaneous effects of the parental variables, the maternal variables generally had stronger effects than the paternal variables on the direct neonatal measures. Figure 7.14 compares the effects on birthweight, CH length, head circumference, AMA and triceps. Patterns with ratio variables were generally less consistent.

Figure 7.14 Maternal and paternal height and BMI effects on neonatal measures



There was no convincing evidence of interactive effects between the parental variables.

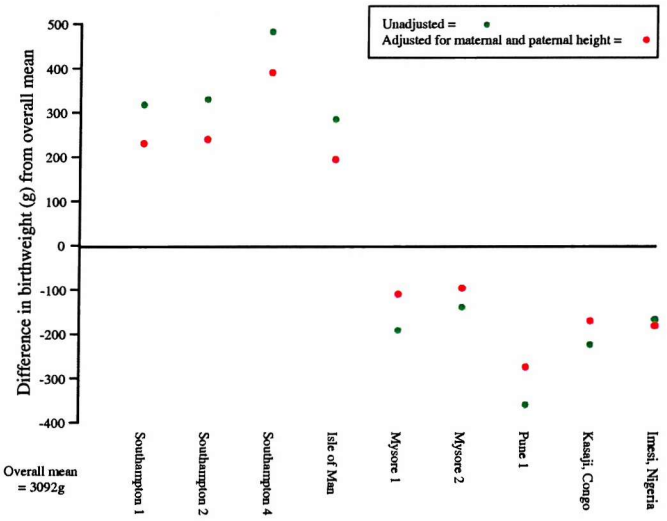
7.3.3 Adjustment for maternal and paternal phenotypes

Maternal and paternal height accounted for up to 5% of the variation in the neonatal measures within each dataset. If the BMIs of both parents were also included, this increased to up to 20%. Dataset location effects on each of the neonatal measures were calculated before and after adjusting for the parental variables.

Height

Before adjustment, neonates were large in the UK, and small in India and Africa compared to the mean values for most measures. These differences were reduced after adjustment for maternal and paternal height, but still existed, as shown in Figure 7.15 using neonatal birthweight as an example. Again, reductions were of a similar magnitude across the datasets.

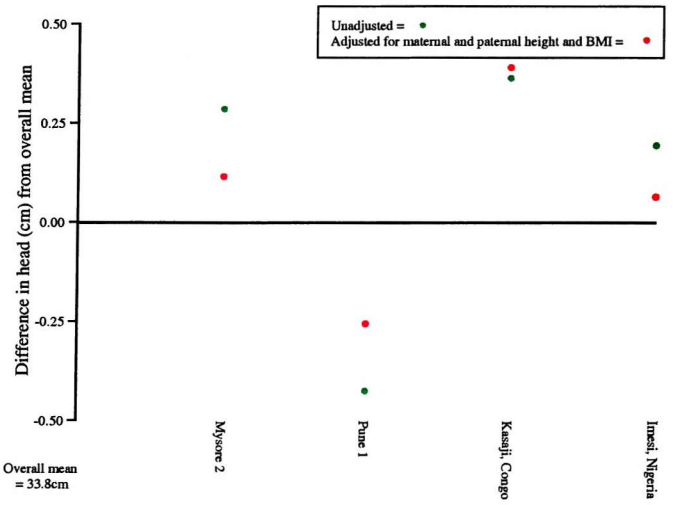
Figure 7.15 Maternal and paternal height and neonatal birthweight



Height and BMI

As the UK datasets were not included in this analysis, dataset effects were generally smaller. However, adjustment for the parental variables still reduced differences between datasets, but less so in Kasaji than India and Imesi. Figure 7.16 shows this for neonatal head circumference.

Figure 7.16 Maternal and paternal height and BMI and neonatal head circumference



Dataset location effects after adjustment for parental variables could not directly be compared with those from §6.4.1, which were based only on adjustment for maternal variables. This was because fewer datasets were used for the current analysis, resulting in altered adjustments for maternal variables. For comparability, the analyses in §6.4.1 were repeated, restricting to datasets that included paternal measurements. Location effects after adjustment for maternal variables were weaker than those shown previously. This was expected as the analyses were based primarily in developing countries, where ranges of maternal variables were narrower.

7.4 Summary

Characterisation of paternal phenotype:

- Fathers from the UK were the tallest, and no measure of BMI was available there. Within India and Africa, fathers from Mysore and Imesi were the largest, with the fattest from Mysore and the tallest from Imesi. The smallest fathers were from Pune and Kasaji, with the thinnest in Pune and the shortest in Kasaji.
- Paternal height and BMI were not correlated in India, although they were positively correlated in Kasaji and negatively correlated in Imesi. However, BMI was found to be a reasonable measure of adiposity based only on these two measures.

Paternal effects on neonatal phenotype:

- Paternal height and BMI each had positive effects on most of the neonatal measures, which were often similar across the datasets. However, relationships between paternal BMI and neonatal birthweight, CH length and chest circumference varied across the datasets due to differences in the African datasets. There were also negative relationships between paternal height and neonatal PI in some datasets.
- Paternal height had the strongest effect on neonatal length, while effects of paternal BMI were generally similar across the neonatal measures.
- Differences in neonatal measures between populations remained after adjustment for paternal height and BMI, although they were reduced to a similar degree in each dataset.

Comparison of maternal and paternal effects on neonatal phenotype:

- Parental heights were correlated in most developing countries, as were parental BMIs, particularly in India.
- Maternal height had a stronger effect than paternal height on most of the direct neonatal measures. However, the effect of paternal height was stronger for most of the neonatal measures in Mysore 2, and some in Pune 1. Comparisons of parental height were less consistent for PI and the ratio variables.
- When considering both height and BMI, the maternal variables generally had stronger effects on the direct neonatal measures than the paternal variables. Again, patterns were less consistent for the neonatal ratio variables.
- Adjustment for both maternal and paternal variables reduced differences in neonatal values across populations, although they still remained.

Therefore, although much less data were available for fathers than mothers, it has been shown that geographical differences in their phenotypes existed both between and within countries. However, relationships between paternal and neonatal measures were generally similar across the datasets, with paternal height having a stronger effect on neonatal length than the other measures. The variation in paternal phenotypes across populations explained some of the geographical differences in neonatal phenotypes. When comparing with maternal effects on neonatal outcomes, most paternal effects were weaker.

8 Relationships with later blood pressure

Systolic blood pressure (SBP) measurements were recorded for subjects either during childhood or adult life in eight of the datasets in the main study, and five in the WHO study. Table 8.1 shows the number of subjects that had an SBP measurement in each of these datasets in the second column, and the percentage of the original dataset excluded in the third column. The Mysore dataset spanned a wide age range (4 to 59 years), and there were no subjects with blood pressure measurements aged between 11 and 19. Therefore it was split into separate datasets for children (Mysore 1a) and adults (Mysore 1b).

Table 8.1 Datasets used for analysis

Dataset	Number	% of original dataset excluded	Difference in values (SBP compared to no SBP)	Age range (years)	% males
Preston	347	65.8%		46-54	49.0%
Sheffield	281	93.6%	+90g birthweight	50-75	53.4%
Farnborough	335	80.0%		20-24	47.2%
Aberdeen	233	0.0%		38-44	48.5%
Mysore 1a	660	} 14.3%	} -115g birthweight	4-10	53.3%
Mysore 1b	400		-0.5cm CHL	20-59	54.3%
Beijing	562	76.9%	-10g placenta	41-47	48.8%
Kingston 1	323	34.1%		2-3	44.9%
Kingston 2	70	0.0%		10-12	51.4%
WHO Sweden	336	33.5%		2-6	51.8%
WHO Chile	361	47.5%	+110g birthweight +0.4cm CHL +0.3cm head	3-5	51.0%
WHO Guatemala	115	60.9%		2-5	53.9%
WHO China	346	36.0%		2-5	54.0%
WHO Nigeria	291	43.2%		2-6	54.0%

Very high proportions were excluded in Preston, Sheffield, Farnborough and Beijing as these datasets comprised all births, not just those traced in later life. The fourth column of Table 8.1 shows which neonatal measurements were significantly different between those who had SBP recorded and those who did not.

Firstly, the effects of possible confounders on SBP were investigated, including height, BMI and room temperature at the time of measurement. Then SBP levels were compared across the datasets. After checking assumptions of linearity, some of the techniques from previous analyses were implemented to investigate geographical variation in relationships

between both neonatal and maternal measures and later SBP levels. Finally, the extent that geographical differences in SBP levels were explained by differences in neonatal and/or maternal phenotypes was considered.

Neonatal measurements selected for analysis were birthweight, placental weight, CH length, head circumference, PI, head to length ratio and placenta to birthweight ratio, which were all adjusted for gestation. There were no other measures that were recorded in enough datasets to be of use. For the mothers, height and BMI (30-week gestation) were the only variables recorded in enough datasets to be used in these analyses. As paternal measurements were only recorded in Mysore, these were not included. It was not possible to investigate the effects of placental weight in Mysore 1b as only nine subjects had values recorded. In addition, effects of maternal BMI on SBP could not be investigated in either of the Mysore datasets as there were no measurements recorded for the children, and only 20 for the adults.

The final two columns of Table 8.1 shows the age range and sex distribution in each of the datasets. Since SBP is strongly related to age (Pickering 1972), and the age range both within and between datasets was so variable, age and sex specific SD scores were used for all analyses, rather than absolute SBP levels. The following formula was used to derive these:

$$\text{SBP SD score} = \frac{\text{SBP - mean}}{\text{SD}}$$

where the mean and SD values were based on external standards.

The only SBP standards that exist for the entire range of ages in the study datasets are from the USA. Means and SDs for males and females separately for each year of age from 1 to 17 were derived from a total of 76,018 SBP measurements from 56,108 children in nine states in the USA (Rosner et al. 1993). These comprised eight states from the Second Task Force on Blood Pressure Control in Children that took place in 1987, and an additional study from Minnesota completed in 1991. Values for those above 17 years of age were derived for age groups of five to ten years, from males and females that took part in the National Health and Nutrition Examination Survey in the USA which involved 65 locations (NCHS 1989). In total, 17, 796 subjects were involved, although this included

those from age 7 upwards. The data were collected between 1971 and 1974. The complete sets of standards are shown in Appendix 6a.

8.1 Effects of confounders on blood pressure

The subject's height and BMI at the time of SBP measurement were recorded for the majority of subjects, and room temperature was generally recorded, except in Jamaica. These variables were normally distributed, and Table 8.2 shows the mean and SD values for each dataset.

Table 8.2 Subject's height and BMI and room temperature – mean (SD)

Dataset	Height (cm)	BMI (kg/m^2)	Room temperature (°)
Preston	165.2(9.4)	26.6(4.5)	20.6(3.3)
Sheffield	165.3(9.1)	27.2(4.5)	18.6(2.8)
Farnborough	170.5(9.1)	23.5(3.7)	21.5(2.4)
Aberdeen	166.7(9.2)	25.8(4.8)	21.1(2.7)
Mysore 1a	117.5(9.0)	13.7(1.4)	27.5(2.1)
Mysore 1b	160.3(9.2)	23.9(4.7)	26.2(1.5)
Beijing	166.4(8.2)	24.0(3.2)	23.5(2.7)
Kingston 1	96.4(3.6)	15.6(1.4)	
Kingston 2	146.7(7.2)	16.6(2.4)	
WHO Sweden	106.7(7.5)	16.0(1.3)	23.5(1.1)
WHO Chile	100.8(6.1)	16.8(1.7)	24.1(4.0)
WHO Guatemala	99.5(7.8)	16.1(1.5)	25.5(2.9)
WHO China	98.7(7.1)	14.6(1.7)	16.0(4.5)
WHO Nigeria	99.6(7.6)	15.2(1.3)	29.3(1.7)

The subject's height and BMI were not significantly correlated in the UK datasets ($|r| < 0.07$ for all where $|r|$ = absolute correlation). However, they were significantly correlated in the remaining datasets in the main study, with r values of 0.29 ($p<0.001$) in Mysore 1a, -0.17 ($p<0.001$) in Mysore 1b, 0.10 ($p=0.10$) in Beijing, 0.32 ($p<0.001$) in Kingston 1 and 0.29 ($p=0.02$) in Kingston 2. In the WHO study, absolute correlations were less than 0.08 except in China ($r=-0.22$, $p<0.001$) and Nigeria ($r=-0.24$,$p<0.001$).

The effects of the subject's height, BMI and room temperature at the time of measurement on SBP were investigated using regression. Individual relationships were assessed using F tests and Appendix 6b shows the linear regression coefficients and, if appropriate quadratic coefficients colour coded according to the strength of their significance.

The subject's height was positively related to SBP in most datasets. However, there was a negative linear relationship in the Mysore adults, and a strong positive quadratic relationship in Aberdeen. In Sheffield and the Mysore children, height was not related to SBP.

Positive linear relationships were seen between the subject's BMI and SBP in most datasets. However, in Aberdeen and the Mysore children, there were negative quadratic relationships, and in Sheffield and WHO China there was no relationships.

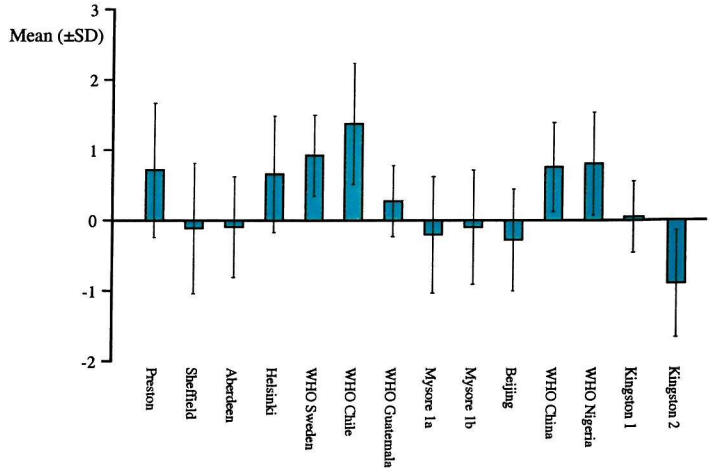
There were inconsistent relationships between room temperature and SBP. A positive linear relationship was seen in Aberdeen, while negative linear relationships were seen in Farnborough, Mysore and China. There were no other significant relationships.

As the subject's height, BMI and room temperature at the time of measurement were related to SBP levels in many of the datasets, the age and sex-specific SD scores were adjusted for these variables for all further analyses. Adjustments were made using regression, and were calculated for each dataset separately.

8.2 Blood pressure levels across populations

Figure 8.1 shows the mean age and sex-specific SD scores for SBP, adjusted for height, BMI and room temperature in each dataset. Tables of mean values can be found in Appendix 6c.

Figure 8.1 Mean SBP measurements (SD scores)



The highest values were seen in Preston, Helsinki, and the WHO datasets except Guatemala, while the lowest were seen in Kingston 2. In the remaining datasets, values were all within ½ SD of the standard population.

8.3 Linearity of relationships with blood pressure

Linearity of the relationships between each neonatal/maternal measurement and later SBP was assessed using F tests. Appendix 6d shows the linear regression coefficients, after adjustment for neonatal sex and gestation.

Birthweight was inversely related to SBP in most datasets, and reached significance in Preston, Farnborough, Aberdeen, Beijing, Kingston 1, and WHO Guatemala. However, there was a u-shaped relationship in WHO Chile (p=0.03), such that those with birthweights at the extremes of the distribution had the highest SBP values. Inverse relationships with SBP were also seen for CH length in WHO Guatemala, head circumference in Farnborough, WHO Chile, WHO Guatemala and WHO China and PI in Preston, Beijing and WHO Sweden. SBP was directly related to the placenta to birthweight ratio in Preston. For the maternal variables, height was inversely linearly related to SBP in Beijing, and those with mothers at the extremes of the height distribution had the highest SBP values in the Mysore adults dataset (p=0.02). BMI was directly related to SBP in Farnborough and Beijing. There were no other significant relationships between the neonatal/maternal variables and later SBP.

8.4 Geographical variation in relationships with blood pressure

Firstly, each pair of neonatal/maternal measurement and later SBP was compared across datasets. Then the effects of different combinations of neonatal/maternal variables on SBP were compared within each dataset.

8.4.1 Individual relationships

The individual effects of neonatal/maternal measures on SBP were compared across the datasets. In a series of separate graphs for each pair, regression lines were plotted for each dataset. F tests were used to investigate whether the relationships in each dataset could be

represented by a common slope. If this was the case, further F tests were used to see if a common intercept could also be used. All neonatal variables were adjusted for gestation. The first column of numbers in Table 8.3 shows whether each relationship could be represented by a common slope, with p-values colour coded according to significance. The number of datasets used for each analysis is shown in brackets. The last column shows the range of estimates if separate slopes were required, or the common slope estimate if there were no significant differences in slopes.

Table 8.3 Common slopes for each pair of measurements

p≥0.1 p<0.1 p<0.05 p<0.01

Neonatal/maternal predictors		SBP (SD score) P-value for common slope *(number of datasets)*	Slope estimate
Neonatal	Birthweight (kg)	0.05 *(14)*	-0.35 to 0.05
	Placental weight (kg)	0.9 *(8)*	-0.31
	CH length (10 cm)	0.3 *(13)*	-0.10
	Head (10 cm)	0.7 *(13)*	-0.20
	PI (kg/m^3/10)	0.1 *(13)*	-0.04
	Head/length (ratio)	0.9 *(13)*	-0.02
	Placenta/birthweight (ratio)	0.2 *(8)*	0.48
Maternal	Height (m)	0.6 *(12)*	-0.41
	BMI (kg/m^2/10)	0.2 *(5)*	-0.003

Common slopes were acceptable for most neonatal measures and both maternal height and BMI, as there were generally no relationships with later SBP. Figures 8.2 and 8.3 demonstrate this for neonatal head circumference and maternal height respectively.

Figure 8.2 Neonatal head circumference and SBP

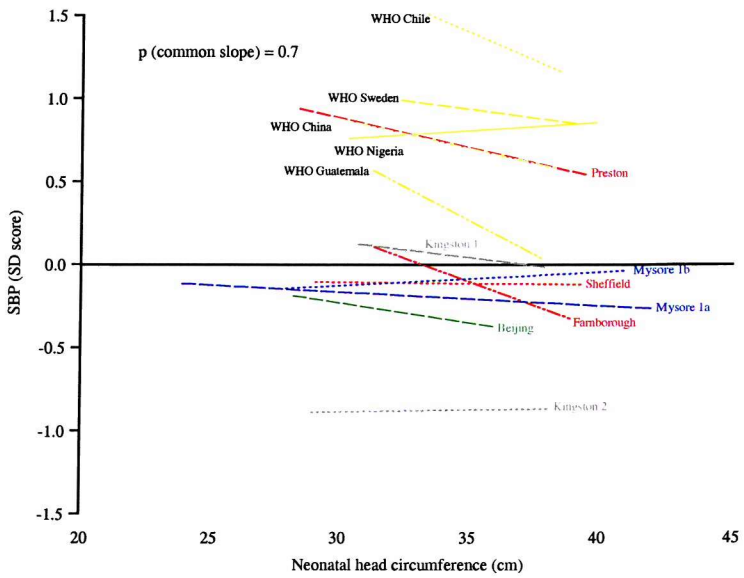
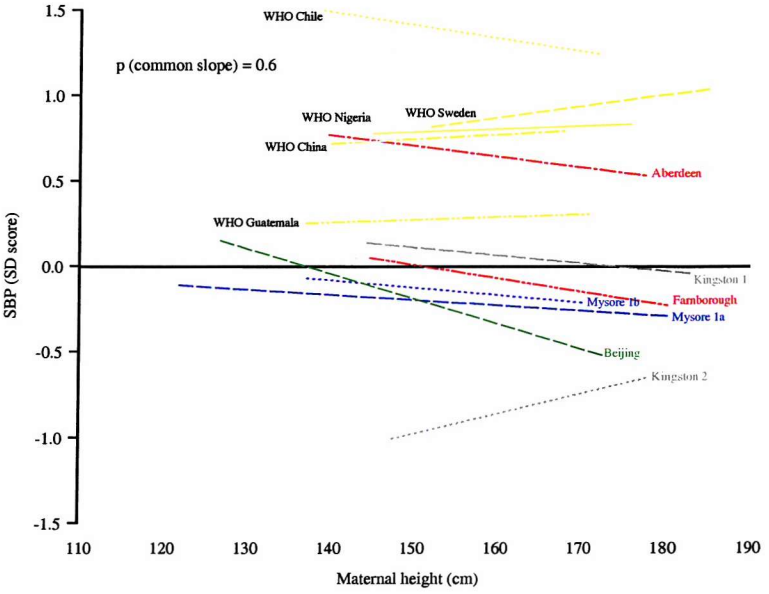
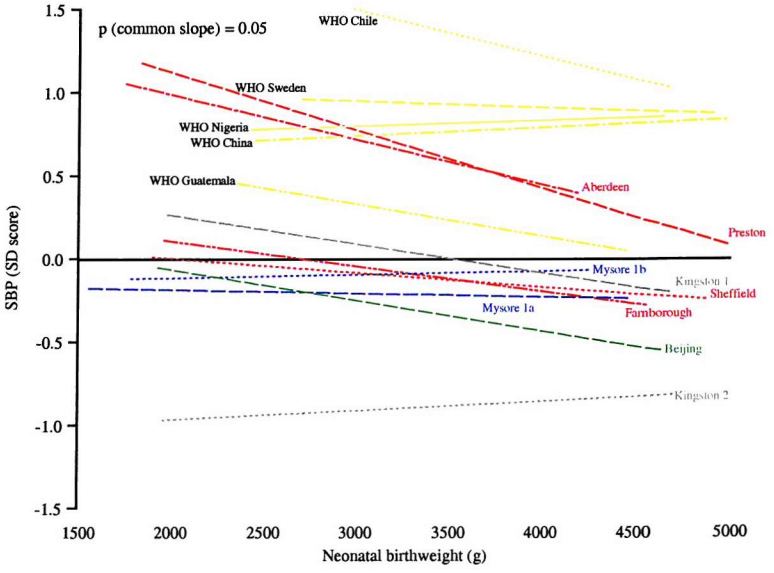


Figure 8.3 Maternal height and SBP



The only exception was the relationship between neonatal birthweight and SBP, as this varied across the datasets as shown in Figure 8.4.

Figure 8.4 Neonatal birthweight and SBP



This was because there were negative relationships in many of the datasets, and no relationships in others.

For all relationships where a common slope was adequate, different intercepts were required for each dataset. In general, similar results were obtained if adjustment was also made for sex, maternal age at delivery and parity.

It was of interest to investigate whether differences in the relationships between neonatal birthweight and later SBP could be explained by differences in neonatal shape across the datasets. Principal components (PCs) were calculated using neonatal birthweight, CH length and head size, based on the same coefficients as for §4.1.3. The mean PC1 (overall neonatal size) and PC2 (contrast between head and length) values for each dataset were plotted separately against the slopes derived from a regression of SBP on neonatal birthweight (Figure 8.5a and b).

Figure 8.5a PC1 and slope (regression of SBP on birthweight)

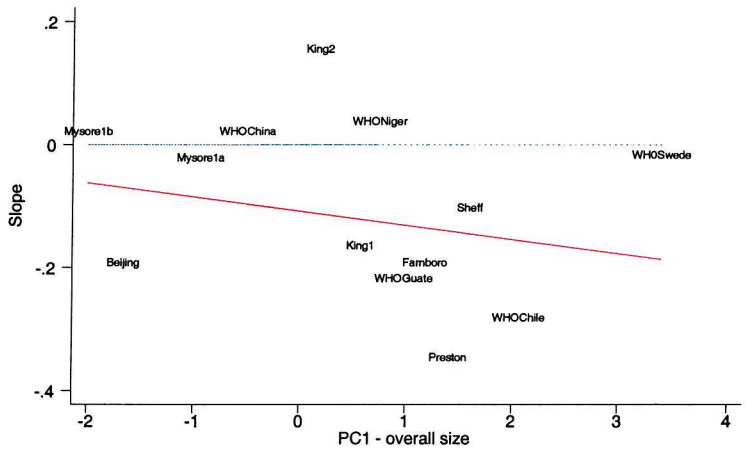
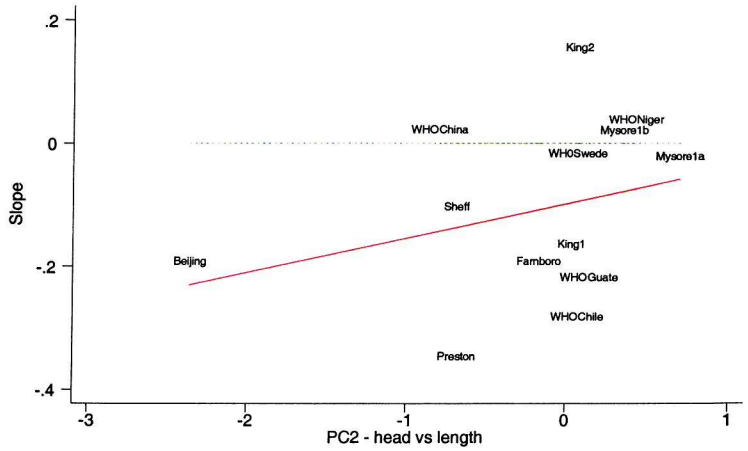


Figure 8.5b PC2 and slope (regression of SBP on birthweight)



The green lines indicate zero i.e. no relationship between birthweight and later SBP, and the red lines are the regressions of the slope on the PC, using univariate models weighted for the number of observations used to derive each slope. Regression coefficients were –0.023 (p=0.3) for Figure 8.5a and 0.056 (p=0.2) for Figure 8.5b. Hence the strongest inverse relationships between birthweight and later SBP were seen in datasets where babies were larger overall, and also in those where babies had small heads compared to their lengths. P values did not reach significance, but this may have been due to the small number on which they were based (n=13). The first and second PCs explained 8% and 17% of the variation in the slopes (regressions of SBP on birthweight) respectively.

8.4.2 Comparison across neonatal and maternal measurements

The simultaneous effects of different combinations of neonatal and maternal measures on SBP were compared within each dataset. The following combinations were used for this analysis, as not all variables were measured in all datasets:

1) Birthweight, placental weight
2) Birthweight, placental weight, CH length, head circumference
3) Maternal height, maternal BMI
4) Birthweight, placental weight, maternal height, maternal BMI
5) Birthweight, placental weight, CH length, head circumference, maternal height, maternal BMI.

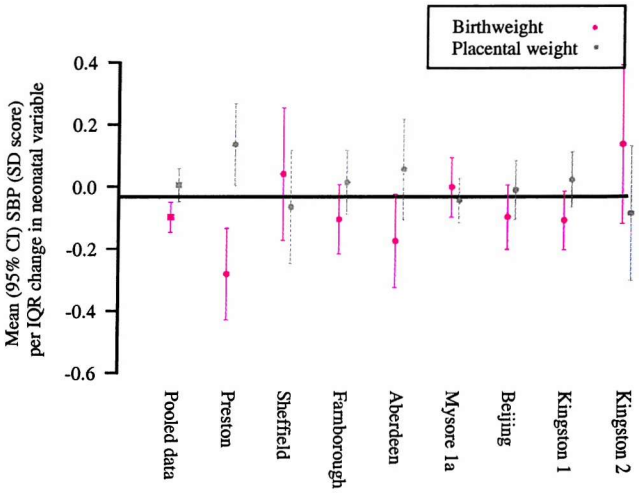
Graphs were constructed to illustrate the effect of an increase the size of the IQR in the neonatal/maternal measure on SBP, after adjusting for neonatal sex. Further details of this method were given in §6.3.4. Table 8.4 shows the IQRs for the neonatal and maternal variables.

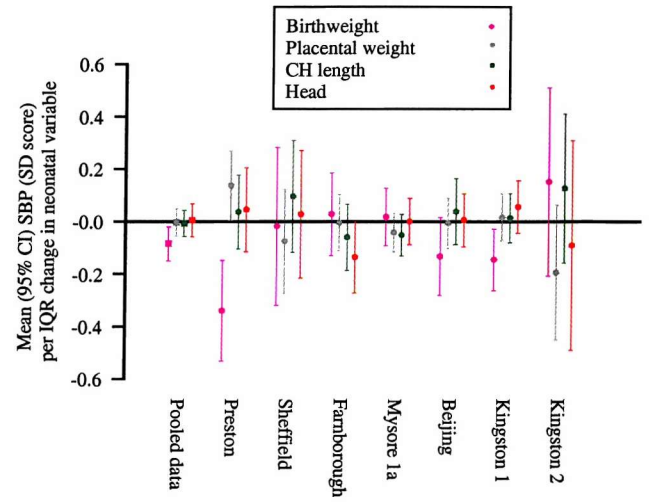
Table 8.4 IQRs for neonatal and maternal variables

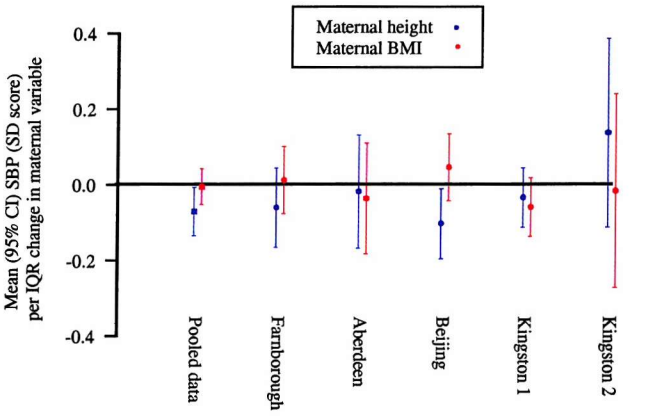
	Neonatal Birthweight (kg)	Placenta (kg)	CH length (cm)	Head (cm)	Maternal Height (cm)	BMI (kg/m^2)
Pooled data						
Set 1	612	145				
Set 2	614	134	3.4	2.5		
Set 3					10.0	4.2
Set 4	530	132			10.0	4.2
Set 5	538	122	3.0	2.7	9.1	4.4
Individual data						
Preston	604	134	2.9	2.2		
Sheffield	739	143	3.5	2.3		
Farnborough	517	116	3.4	1.8	8.3	3.8
Aberdeen	529	142			7.6	3.4
Mysore 1a	568	70	3.3	1.9		
Mysore 1b						
Beijing	536	96	2.4	1.8	7.0	2.9
Kingston 1	572	136	3.5	1.7	8.3	6.3
Kingston 2	614	101	4.4	2.9	8.0	4.5

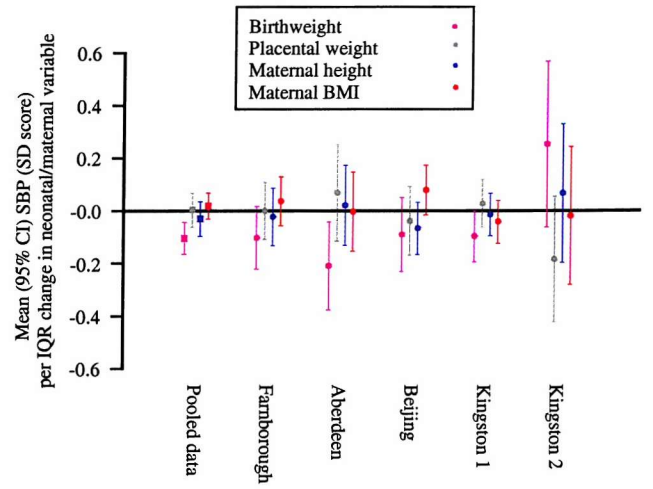
Figure 8.6 shows the effects of the each of the five combinations of neonatal and maternal measures on SBP. The simultaneous effects of the measurements are plotted, although individual effects were similar.

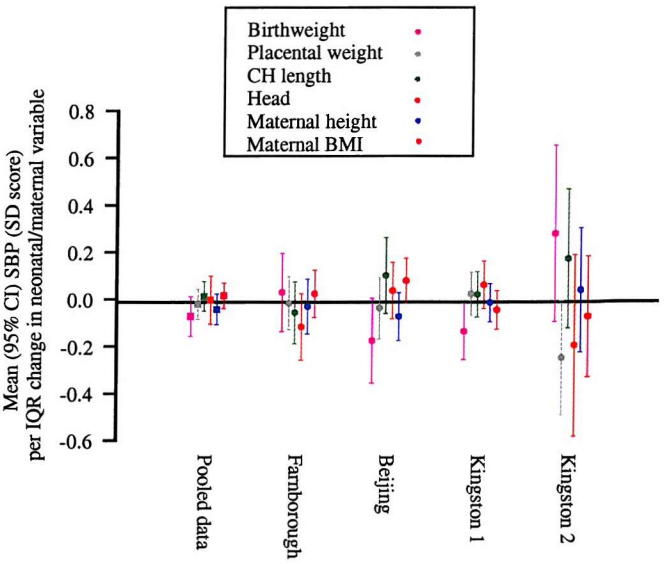
Figure 8.6 Neonatal/maternal measures and SBP




Birthweight
Placental weight
CH length
Head
Mean (95% CI) SBP (SD score) per IQR change in neonatal variable
0.6
0.4
0.2
-0.0
-0.2
-0.4
-0.6
Pooled data
Preston
Sheffield
Farnborough
Mysore 1a
Beijing
Kingston 1
Kingston 2


Maternal height
Maternal BMI
Mean (95% CI) SBP (SD score) per IQR change in maternal variable
0.4
0.2
0.0
-0.2
-0.4
Pooled data
Farnborough
Aberdeen
Beijing
Kingston 1
Kingston 2


Birthweight
Placental weight
Maternal height
Maternal BMI
Mean (95% CI) SBP (SD score) per IQR change in neonatal/maternal variable
0.6
0.4
0.2
-0.0
-0.2
-0.4
-0.6
Pooled data
Farnborough
Aberdeen
Beijing
Kingston 1
Kingston 2


Birthweight
Placental weight
CH length
Head
Maternal height
Maternal BMI
Mean (95% CI) SBP (SD score) per IQR change in neonatal/maternal variable
0.8
0.6
0.4
0.2
0.0
-0.2
-0.4
-0.6
Pooled data
Farnborough
Beijing
Kingston 1
Kingston 2

In most datasets, neonatal birthweight had the strongest effect on SBP, whatever other neonatal and maternal measures were considered. Effects of maternal height and BMI on SBP were weaker, and generally similar in magnitude.

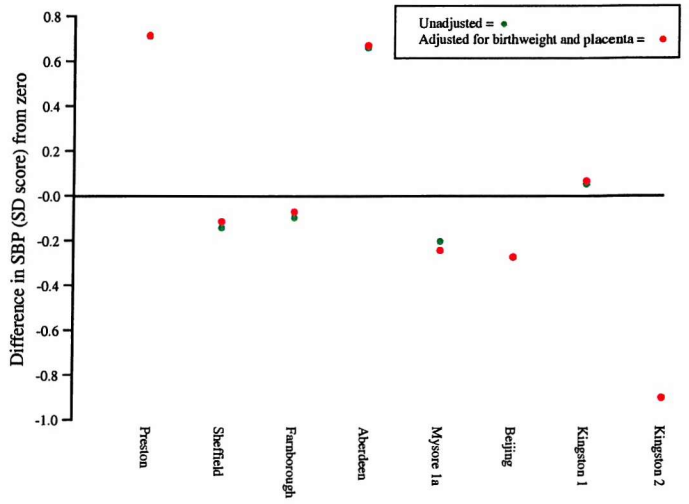
There was no convincing evidence of interactions between the neonatal and maternal variables.

8.5 Comparison of blood pressures if similar neonatal/maternal phenotypes

The effects of the dataset locations on SBP in childhood or adulthood, before and after adjusting for the different combinations of neonatal and maternal variables outlined at the start of §8.4.2 were investigated. 'Constrained regression', as described in §6.4.1 was used. However, all regression models were constrained for the constant to equal zero, as mean SBP SD values were very close to zero for each set of pooled data. Also, neonatal and maternal variables were used as continuous variables, as all relationships with SBP were linear and there were very few interactions. They were centred to allow calculation of true dataset location effects after constraining the model constant to equal zero. However, as the proportion of variance in SBP explained by the different combinations of neonatal and maternal variables was less than 5% in most datasets, it was not expected that these combinations of variables would account for much of the variation in SBP levels across populations.

Figure 8.7 shows the change in SBP SD scores after adjusting for neonatal birthweight and placental weight for each dataset. The green dots are hidden by the red dots in some datasets.

Figure 8.7 Neonatal birthweight and placental weight and later SBP



Hence adjusting for neonatal birthweight and placental weight make very little difference to the mean SBP SD scores in each dataset. Similar results were obtained if adjustments were made for the other four sets of neonatal/maternal variables.

8.6 Summary

Effects of confounders on blood pressure:

- The subject's height and BMI at the time of blood pressure measurement were generally positively related to SBP levels. Relationships with room temperature were inconsistent across the datasets.

Blood pressure levels across populations:

- The highest SBP levels were seen in Preston, Helsinki and all the WHO datasets except Guatemala, while the lowest values were seen in Kingston 2.

Geographical variation in relationships with blood pressure:

- For most neonatal measures and also maternal height and BMI, relationships with SBP were generally weak, and common slopes for all datasets could be used to summarise them. However, relationships between birthweight and SBP varied across the datasets; in many there were negative relationships while in others these variables were not related. The strongest inverse relationships with birthweight were seen in datasets where babies were larger overall, and also in those where babies had small heads compared to their lengths, although these findings did not reach significance.
- Amongst the neonatal and maternal measures, neonatal birthweight had the strongest effect on SBP in most datasets. Effects of maternal height and BMI were weaker, and were similar in magnitude.

Comparison of blood pressure if similar neonatal/maternal phenotypes:

- Adjustment for neonatal and/or maternal variables did not reduce differences in SBP levels across populations.

9 Discussion

The main findings of the thesis will be discussed in the context of the literature available, and limitations of the data and analysis methods commented upon. Implications of the results and possible future work will be suggested.

9.1 Summary of thesis

Studies demonstrating a relationship between small size at birth and adult cardiovascular disease suggest that reducing adult disease requires an improvement in fetal growth. The size and body proportions of the baby at birth are partly determined by maternal size and body composition. Information on geographical variation in body proportions other than birthweight in neonates and height and weight in mothers has not been well documented.

This thesis has compared the size and shape of neonates across a number of populations, including the UK (four Southampton datasets, Preston, Sheffield, Farnborough, Isle of Man, Aberdeen), Finland (Helsinki), India (two Mysore datasets, two Pune datasets), Sri Lanka (Kandy), China (Beijing), Congo (Kasaji), Nigeria (Imesi) and Jamaica (two Kingston datasets). In addition, seven datasets from a WHO study based on normal birthweight neonates were also used for some analyses. The size and shape of mothers have been compared, and maternal-neonatal relationships investigated in detail in many of the populations.

As paternal size also plays a role in determining fetal growth and present literature in this area is scarce, paternal-neonatal relationships have been compared with maternal-neonatal relationships where possible. Finally, the analyses have been extended to investigate whether differences in neonatal and/or maternal body composition can explain differences seen in relationships with blood pressure in later life in datasets with measurements available.

9.2 Main findings

9.2.1 Characterisation of neonatal phenotypes

The main findings regarding characterisation of the neonatal phenotypes across the datasets are outlined on pages 89-90. There were a number of differences between the populations, which can be summarised as follows:

- Overall size
- Head size (Beijing reduced compared to other populations)
- Components of length (short legs and long bodies in Beijing, long legs and short bodies in Mysore)
- Fat preservation (India compared to other populations)
- Head to length ratio.

For most individual measurements, neonates in Europe and Australia were the largest, followed by those from Jamaica, Chile, Guatemala and China, then Africa, India and Sri Lanka (Figure 4.5). For example, birthweight fell from approximately 3500g in Southampton to just over 2700g in rural India and Sri Lanka.

Although there was generally least variation in the skeletal measurements across the populations, the neonates in Beijing had markedly reduced head size. This may have been due to measurement error as data were taken from obstetric records, and without a protocol to follow, midwives might not have selected the widest part of the head to measure. However, in the WHO data, where a standardised protocol was used in all centres, head size in China was smaller than in the other six datasets, which allows the finding to be asserted with more confidence (Figure 4.13). In addition, Meredith (1971) has also shown neonatal head size in China to be among the smallest when compared to a number of other populations.

There was a strong contrast between the length components of trunk and leg in Beijing and Mysore 2. The Chinese neonates had short legs and long bodies, while the Indians had long legs and short bodies. As discussed above, there may have been measurement error in the Beijing data, as these were based on obstetric records, but the Mysore data were based on clinic measurements made by trained observers, so are likely to have been of high quality. However, as no other datasets from China or India included measurement

of the length components, it was not possible to establish whether these patterns were characteristic of the populations.

In the Indian neonates, fat was less reduced than other measures of body composition. This finding was based on three high quality datasets from Mysore and Pune. Yajnik (2001) proposed that this reflects a 'thrifty phenotype', whereby Indian neonates preserve fat at the expense of muscle in utero, and it is the subscapular skinfold rather than triceps that is preserved, i.e. central fat. Hediger et al. (1998) and Yajnik et al. (in press) also demonstrated relative fat preservation in small for gestational age neonates in the USA and UK respectively, although to a lesser extent.

The main difference in neonatal shape between populations when considering only birthweight, length and head circumference (available in most studies) was in the head to length ratio. Neonates in India, Sri Lanka and Africa had large heads while those in China had small heads compared to their length. This was found using both star graphs and principal components analysis (§4.1.3), based on mean values from each dataset in the main study. In the WHO datasets, differences in shape were consistent with those found in the main study datasets, although were less distinct. This was likely to be because there were no low birthweight neonates by design, so the ranges of measurements were reduced. It is also possible that some of the differences in the main study may be due to difficulties with comparability of samples and measurements. However, as similar patterns were seen within the European datasets and within the Asian datasets, this allowed more confidence in the findings. Only two other studies have attempted this type of analysis (Denham et al. 2001, Hindmarsh et al. 2002), although each was based on results within rather than across populations. For both, measures of muscle and fat were included in addition to birthweight, length and head circumference. The first two components in Denham's analysis based on term babies in the USA explained 84% of the variation in the data, while in Hindmarsh's analysis based on term babies in the UK, they explained 73% of the variation. In both studies, the first component represented overall size, and the second represented a contrast between skeleton (length and head) and fat (skinfolds), i.e. neonates with higher values on this component were longer and thinner than those with lower values who were shorter and fatter. The comparatively high proportion of variance (94%) explained by the first two components in the current study is likely to have been due to the small number of original variables used. For each of the Southampton, Mysore, Pune and Kasaji datasets, it was possible to repeat the analysis including MUAC and subscapular

skinfold (Appendix 2b). The first two components explained 78% to 85% of the variance in each dataset, and had similar interpretations to those derived in the Denham and Hindmarsh studies.

There are many reasons why neonates may vary in size and shape across populations. Undernutrition is likely to play an important role, and mothers in each population are likely to be exposed to different diets and social conditions, resulting in differing supplies of nutrients to their fetuses. It has been speculated that growth retardation of different body proportions at birth is due to the timing of undernutrition in utero (§1.3.3). For example, if the Chinese mothers were undernourished in the first trimester, their babies' heads would have been small, as the head is established first. They may then have adapted to undernutrition throughout gestation, so would not be depleted in muscle or fat. Other growth retarded babies such as those in India may have been undernourished later in gestation, so their heads grew adequately and were not substantially smaller than those of Western babies, but length and soft tissues did not, a phenomenon known as 'brain sparing'. Fat preservation at the expense of other tissues in Indian neonates is another possible example of the effects of undernutrition; it may be that in these small neonates inadequate nutrients were received, leading to inefficient use of the available energy, which was deposited as fat at the expense of other tissues (Jackson and Wootton 1990).

In addition to nutritional differences between populations, genetic factors are likely to play a role, as different genes evolve for survival in different populations. Natural selection ensures that some traits are reduced or eliminated while others are reinforced, to produce phenotypes that are capable of living in a particular environment. During the neonatal period mortality is high, hence factors influencing survival at this age have a high selection pressure, such as the ability to metabolise food efficiently and to fight infection. However, the size of a fetus' head is limited by the size of the mother's pelvis that it passes through during birth, although after birth it grows rapidly in the first few months of life. It may be that in China, mothers' have smaller pelvises, and therefore small head size for birth has evolved in this population. This is more likely to be a factor than fetal undernutrition, as there is no evidence that brain function is reduced in China. Another example of a geographical difference between phenotypes that may have a genetic basis is fat preservation in Indian neonates. During the last two months of gestation fat deposition increases rapidly, reaching approximately 16% of neonatal weight by birth, compared to 0.5% at the start of gestation (Widdowson 1970). Blaffer Hrdy (2001) has suggested a

number of reasons for this stockpiling of fat prior to birth, which include the 'food for thought hypothesis', whereby neonatal fat is accumulated to ensure adequate brain development. It may therefore be that Indian neonates have to deposit more fat, as their relatively large heads require extra fat for growth. An alternative is the 'self-advertising hypothesis', based on the idea that neonatal fat makes babies more appealing as it suggests that they have a good chance of survival, although this does not explain why Indian babies have relatively more fat than other populations.

A further area of interest was the use of ponderal index as an index of adiposity. It was not thought to be acceptable as it was not independent of length in most datasets. Hence values were misleading, for example in Kasaji, the PI was similar to other datasets, although direct measurements of fat were substantially smaller. More appropriate indices were derived by finding the power for length that minimised the correlation between the new index and length itself (Table 4.7). In some datasets it was also possible to find indices that reduced correlation with length while simultaneously increasing correlation with fat, based on skinfolds (Table 4.8). However, these new indices could not be used in this study as they required derivation in each dataset and so were not comparable across datasets. Results were based on PI where direct measures of fat were not available, and should be treated with caution. Use of alternative indices could be considered in future studies if they were based only on internal comparisons, although direct measurement of fat would be preferable.

9.2.2 Characterisation of maternal phenotypes

Details on variation in maternal phenotypes across the populations are summarised on page 108. European mothers were generally the largest in most measurements, while those from India and Sri Lanka were the smallest (Figure 5.1). For example mean height and BMI were 164cm and 27 kg/m^2 respectively in Southampton, and 151cm and 20 kg/m^2 respectively in Sri Lanka. There is little information available on geographical variation in maternal size in the literature other than on height, weight and BMI, although these data do support the current study findings (ICMR 1984, Department of Health 2000).

Apart from overall size, the main difference between the mothers was the amount of fat relative to muscle (§5.3). Mothers from urban India had more fat, while those in rural

India, Africa and Jamaica had less fat relative to muscle. This is not surprising, as the factors that determine adult fat and muscle are likely to differ across populations. For example, activity levels have a strong influence on fat and particularly muscle, and women in rural areas in developing countries may have to undertake strenuous physical work that is less common in urban areas. Diet has an important effect on levels of body fat, and again this is likely to vary across populations.

Genetic as well as environmental factors are likely to contribute to the geographical differences in maternal body composition between populations. It may be that women from developing countries are genetically programmed to be small, and studies of migration and secular trends can be used to investigate this. For example, two studies (Draper et al. 1995, Margetts et al. 2002) have found that babies of second-generation Asian women born in the UK had similar birthweights to those of first-generation Asian women who were born in the Indian subcontinent. However, in another study (Dhawan 1995), babies of the second-generation Asian women were found to be heavier, suggesting that changing environments can have an effect on birthweight. A comparison of adult size between first and second-generation Asian women would be ideal, but these data do not exist. In the Margetts et al. study, no secular trends in birthweight were found over the past 40 years. In contrast to this, Sachdev (1997) reviewed the nutritional changes that have taken place in India since the 1970s, and concluded that the modest improvements have led to increases in anthropometry and birthweights. Hence the evidence on whether body composition is fixed or can be altered is conflicting.

9.2.3 Mother to baby relationships

The results of the mother to baby analyses are outlined on pages 148-9. All the maternal variables had important positive effects on most of the neonatal measures (§6.3.1). These were often similar across the datasets, although there were stronger relationships with some of the neonatal measures for maternal height, BMI and birthweight in the developing countries, and for maternal AMA in Kasaji. However, in Kingston 2, both maternal BMI and triceps had negative effects on CR length, in contrast to strong positive effects on leg length. As this dataset was much smaller than the others, these findings cannot be asserted with much confidence.

The effects of the maternal variables on neonatal measures were not weakened by simultaneous adjustment, with the exception of maternal head circumference. This effect was substantially reduced, possibly because it was highly correlated with the other maternal measurements in each dataset (Table 5.8). However, the head effect was not weakened to such an extent in Pune 1 where correlations with other maternal measurements were the weakest.

Within each dataset, the magnitude of the effects of maternal height and BMI were similar for many of the neonatal measurements (§6.3.3). However, BMI had a stronger effect than height on neonatal birthweight in Mysore 2. This may be because the mothers in Mysore were relatively fat but short in height, and their shortness may reflect undernutrition earlier in their own lives. It may therefore be difficult for them to grow their baby's skeleton, although still possible to transmit fat. A large number of studies have found weight to have a stronger effect than height. For example, in a meta-analysis based on 25 studies in both developed and developing countries, maternal weight was found to be the strongest predictor of neonatal birthweight (WHO 1995). However, as weight was used rather than BMI, the measurement was not independent of height. Also, neonatal birthweight was used as a dichotomous variable with 2500g as the cutpoint, and maternal weight was categorised into four groups, resulting in loss of information. Other studies may have findings that contradict those in the current study if they did not restrict to singleton term births and adjust for gestation and other confounders, and also neonatal birthweight was often the only outcome considered. Differing results may also be due to the method of analysis. Neggers et al. (1995) commented that no studies have previously quantified and compared the independent effects of various maternal anthropometric measurements on various neonatal anthropometric measurements. When regression analysis is based on unit change in the maternal variables, effect sizes cannot be compared across variables.

In general, 'like with like' relationships were seen for maternal height, head and fat, i.e. maternal height was the strongest predictor of neonatal length, maternal head the strongest predictor of neonatal head, and maternal fat the strongest predictor of neonatal fat. This may be expected from what is known about genetics, for example, if a mother is taller she is more likely to have a tall child. Environment is also important, as tall mothers are themselves likely to have been adequately nourished during childhood, and so are able to provide adequate nutrition for their babies. Few studies in the literature have considered

maternal measurements other than height and weight and their effect on neonatal birthweight. However, maternal height to neonatal length relationships have been shown (Sibert et al. 1978, Neggers et al. 1995), as have maternal to neonatal fat relationships (Whitelaw 1976, Frisancho et al. 1977, Sibert et al. 1978, Swain et al. 1991, Neggers 1995, Silliman and Kretchmer 1995), although only Neggers et al. compared the effects of several maternal variables on each neonatal outcome and demonstrated that maternal height was one of the strongest predictors of neonatal length, and maternal fat was one of the strongest predictors of neonatal fat using skinfolds. Maternal head circumference has only been measured in very few studies, and relationships with neonatal head have not been examined.

Maternal muscle was not the strongest predictor of neonatal muscle in any of the datasets except Kasaji. This was possibly because only indirect measures of muscle could be used for the neonates. MUAC contains bone and a layer of fat as well as muscle, and while use of AMA overcomes the problem with the inclusion of fat, the formula for derivation is not ideal for neonates, as no correction has been made for the inclusion of bone, unlike the formula used for mothers. The only previous studies that have investigated this relationship are from the USA (Neggers et al. 1995) and Peru (Frisancho et al. 1997). Neggers et al. showed that maternal MUAC was one of the strongest predictors of neonatal MUAC, although not as strong as maternal BMI. Frisancho found that neonates born to mothers with high AMA had higher AMA themselves when compared to those born to mothers with low AMA, although the effect size was not compared to that of other maternal variables.

In the current study, maternal fat tended to have a stronger effect than muscle on the neonatal outcomes in most datasets, especially in Mysore 2. However, the opposite was seen in Kasaji. This may be explained by the Mysore mothers being relatively heavy and fat, while the Kasaji mothers were more muscular. Results in the literature are conflicting, but more studies have shown maternal muscle to have more influence on fetal growth than maternal fat (Langhoff-Roos et al. 1987a, Merchant et al. 1989, Neggers et al. 1995, Frisancho et al. 1997). However, none of these studies assessed effects of the maternal variables using comparable units of measurement, with the exception of Neggers et al. (1995) who calculated effects of changes from the 10^{th} to 90^{th} percentile in the maternal variables.

There was a strong influence of maternal birthweight, particularly in Mysore 2. In a review of the literature, Ramakrishnan et al. (1999) found maternal birthweight to have a stronger effect in Guatemala than in any UK studies. They speculated that stronger relationships in developing countries might be seen because these women inherit inadequate environments across generations, so intergenerational effects may be greater. Another possible environmental factor may be that the effects of the mother's own intra-uterine experience had permanent effects on her adult size, the development of her reproductive organs, or her hormonal and metabolic systems. It may also be that women in some developing countries inherit genes that are more similar across generations than in developed countries due to higher incidences of marriages among relatives i.e. consanguinity. The relationship between maternal birthweight and other body proportions of the neonate have only been investigated in two studies. There were associations with neonatal length in the Guatemalan study, and also a study in the UK (Godfrey et al. 1997) which were both significant, although it was not possible to compare their magnitude due to differences in statistics reported. No studies have compared the size of the effect of maternal birthweight and adult anthropometric measurements using comparable units.

Although differences in neonatal size between populations still remained after adjustment for maternal phenotype, they were considerably reduced (§6.4.1). For example, birthweight differences from the overall mean (based on all populations) were reduced by up to 200g. Hence improvements in fetal growth should follow from nutritional changes that lead to taller maternal stature and greater BMI, although increases in the latter are likely to reach a threshold. Other factors such as maternal diet, physical activity, smoking, alcohol consumption, illness and social class varied across populations, and these along with genetic differences may explain the remaining variation between populations.

Knowledge of individual maternal components such as muscle and fat did not explain geographical differences any better than height and BMI alone. This suggests that measurement of soft tissue at only one location, such as the arm does not distinguish between populations as well as a measure of total mass such as BMI. However, reductions in effect size after adjusting for maternal body composition may differ if other measurements of muscle and fat, such as muscle mass and fat mass had been used.

For mothers of the same height and BMI, neonates still varied across datasets, and for most measurements, particularly for taller mothers (§6.4.2). This can be explained by

taller mothers having more potential for a wide range of size of baby, whereas short mothers are constrained to have smaller babies, otherwise it would be difficult for them to give birth.

9.2.4 Father to baby relationships

It was possible to investigate father to baby relationships in some of the datasets, and results are summarised on pages 166-7. Paternal height and BMI both had positive effects on most of the neonatal measures, which were often similar across the datasets (§7.2.2). However, relationships between paternal BMI and neonatal birthweight, CH length and chest circumference varied across the datasets due to stronger relationships in Kasaji than the other populations. There were also differences in relationships between paternal height and neonatal PI, which may be explained by differing effects of paternal height on length, for example relationships in Southampton 4 were relatively strong compared to weaker relationships in Imesi. This finding contributes to the argument that PI is not a particularly useful measure of adiposity as it is dependent on length.

Paternal height had a stronger effect on length than any of the other neonatal measures, implying that the genetic influence on the skeleton is greater than that on the soft tissues. Godfrey et al. (1997) suggested that this is because the genetic influences associated with paternal height promote high rates of skeletal growth, outstripping the supply of nutrients for soft tissue deposition. Effects of paternal BMI were smaller, and generally similar across the neonatal measures.

Parental heights were correlated in most developing countries, as were parental BMIs, particularly in India, which was expected due to the 'assortative mating' based on stature, which is part of the arranged marriage system (Table 7.5). The maternal measures generally had stronger effects than the paternal measures, whether considering height only (to include the developed countries), or both height and BMI (developing countries only) (§7.3.2). It was probable that paternity had not been confirmed in any of the datasets, and the inclusion of partners who were not the biological fathers may have reduced the size of the paternal effects. Also, it could be argued that it was difficult to compare BMI as the maternal values were derived at 30-weeks gestation so included the weight of the fetus. The small number of studies that have compared maternal and paternal effects have had similar findings (Morrison et al. 1991, Hennessy and Alberman 1998, Klebanoff et al.

1998), although these have all been based in developed countries, and only considered effects on neonatal birthweight. Stronger maternal effects would be expected, as the father's contribution to neonatal size is mainly genetic, while the mother has both genetic and environmental influences. There is debate over the extent of the genetic contribution to fetal growth. Some have suggested it is small, using intergenerational studies (Carr-Hill et al. 1987, Langhoff-Roos et al. 1987b), and studies of siblings and twins (Morton 1955). However, gene markers associated with size at birth have recently been found (Dunger et al. 1998, Vaessen et al. 2002). In addition, a genetic explanation of the relationship between size at birth and adult disease has been proposed by Hattersley and Tooke (1999). Their 'fetal insulin hypothesis' suggests that the genetic mechanisms that regulate insulin secretion and resistance can influence fetal growth, as insulin is a growth factor in prenatal life. In a review article (Frayling and Hattersley 2001), many examples of the role of genes in the association between low birth weight and later NIDDM are given.

Differences in neonatal measures between populations were reduced to a similar degree in each dataset, although remained after adjustment for maternal and paternal measures (§7.3.3). For example, birthweight differences from the overall mean (based on all populations) were reduced by up to 70g after adjustment for parental height and BMI (compared to 60g for maternal variables only, and 30g for paternal variables only, for the same datasets). Hence, as discussed previously, there must be additional factors involved in the determination of fetal growth. It seems unlikely that availability of more detailed measurements of paternal body composition would allow a greater proportion of the variation in neonatal measures across populations to be explained, based on results from detailed maternal body composition measurements.

9.2.5 Relationships with later blood pressure

Relationships with later blood pressure were analysed in datasets where possible, and the main findings are summarised on page 180. Inverse relationships were seen in many datasets between neonatal birthweight and systolic blood pressure in later life, although in some, mainly based on children, there were no relationships (Figure 8.4). In the literature the majority of studies have found inverse relationships (Huxley et al. 2000), although these were weaker in children than adults. A number of possible mechanisms have been suggested as links between low birthweight and higher blood pressure levels in later life.

Fetuses that are undernourished during gestation may make adaptations directed at raising blood pressure to increase placental perfusion (Law and Barker 1994). They may also make adaptations that indirectly raise blood pressure. For example, blood flow may be diverted towards the head to maintain brain growth, leading to less compliance in peripheral blood vessels and therefore higher blood pressure (Martyn and Greenwald 1997). As undernutrition in utero leads to impaired development of tissues that control blood pressure such as blood vessels and kidneys, it may also be that it is not possible for these to recover in later life. For example, the size and number of renal nephrons may be reduced, and the intra-uterine environment is the only opportunity to acquire these (Hinchliffe et al. 1992).

Geographical variation in birthweight to blood pressure relationships in the current study may exist due to differences in timing of undernutrition and hence differences in the adaptations made by the fetus. The strongest inverse relationships with birthweight were seen in datasets where babies were larger overall (based on birthweight, length and head circumference), and hence where the range of birth size was greater (Figure 8.5a). The strongest inverse relationships were also seen in datasets where babies had small heads compared to their lengths (Figure 8.5b), which was not expected from what is known about brain sparing (Martyn and Greenwald 1997). Although these two findings did not reach significance, they explained 8% and 17% of the variation in the relationships between birthweight and later blood pressure across the datasets respectively.

For other body proportions at birth, placental weight and ratio to birthweight, and also maternal height and BMI, relationships with blood pressure were generally weak (Table 8.3). Some studies have investigated relationships with head, length, PI and chest circumference although findings were mainly inconsistent (Huxley et al. 2000, Law et al. 2000); relationships with neonatal fat or muscle have not been considered. Similarly relationships with placental weight or placenta to birthweight ratio have also been inconsistent (Godfrey 2002). A small number of studies have considered maternal size effects on their offspring's blood pressure, and relationships were generally not seen after adjustment for the current size of the offspring (Whincup et al. 1992, Bergel et al. 2000).

Adjustment for neonatal and/or maternal variables did not reduce differences in blood pressure levels across populations (§8.5). This was not surprising as, with the exception of neonatal birthweight, the measures of size and body composition were only weakly

related to later blood pressure levels. It would be useful to repeat these types of analysis using childhood and adult outcomes that are more strongly related to size at birth, such as hypertension, diabetes and CHD.

9.2.6 Placental trimming study

An additional part of the thesis was to investigate the placental weight measurement, which had been used in many of the analyses. As there is no standard technique for preparing the placenta for weighing, comparisons of absolute values across datasets would have been problematic. No previous study has systematically quantified the magnitude and variability of the contribution of the umbilical cord and membranes to untrimmed placental weight. Woods et al. (1978) presented mean values for untrimmed and trimmed placental weights from South Africa, but did not assess the difference between them. Bolisetty et al. (2002) presented the first published data on weights of umbilical cords, but did not assess these in terms of gross placental weight. Hence a sample of 50 neonates born in Southampton was used to quantify the percentage difference between untrimmed and trimmed placental weight.

The mode of delivery was the only factor of those recorded that affected the percentage difference in weight. Differences were larger for vaginal than caesarean deliveries, and were more marked for the cord than the membranes. To enable easy removal of the placenta, the cord may be cut closer to the baby in vaginal deliveries, resulting in a longer and heavier cord. The mode of delivery may also influence the delay between delivery of the infant and clamping of the cord, and alter the degree to which blood is squeezed out of the placental parenchyma into the cord and infant. In Southampton, cord clamping is generally delayed for at least a minute after both vaginal and caesarean section deliveries. In addition, while Yao et al. (1969) showed that clamping the cord less than a minute after delivery reduced the transfusion of blood into the infant, they found no relation between the time of cord clamping and placental weight.

The correlation between untrimmed and trimmed placental weights was 0.98. Excluding caesarean section deliveries, the difference between these weights was 19% (IQR 16%, 22%), and this value was used to adjust values in datasets where weights were not trimmed. There are some limitations with using this value, in addition to the difficulty with being unable to identify those delivered by caesarean section and applying a different

adjustment to them. As the sample used to derive this adjustment factor included only liveborn singleton infants that were delivered on weekdays between 6am and 6pm with complete placentas and membranes, few with intrauterine growth retardation or macrosomia were included. Also, the adjustment factor was derived from a Western population, but applied to data from India, China and Jamaica where it is possible that the percentage difference may not be the same.

For future studies, use of the adjustment factor would enable fairer comparisons of absolute placental weights between populations to be made, despite the limitations. A number of studies have already investigated associations between placental weight and health in later life. Although preparation of the placenta before weighing has been inconsistent in these studies, this is unlikely to invalidate the findings as untrimmed and trimmed placental weights were so highly correlated.

9.3 Limitations

9.3.1 Comparability of subjects

Datasets were selected for this study if they contained neonatal and maternal anthropometric measurements, and were based on normal populations i.e. not exposed to extreme situations such as famine. However, there are a number of reasons why the subjects included in each dataset may not be representative of those in the population from which they were sampled. Inclusion criteria may have involved restrictions on maternal age, marital status, parity and literacy, and varied across datasets. In addition, recruitment into datasets varied from pre-pregnancy through different stages of gestation, until after delivery. This may have introduced bias, for example mothers in the Pune 1 dataset enrolled before pregnancy, and as this made them more aware, this could be considered an intervention. Mothers that were recruited early in pregnancy were likely to have been more motivated, or have had a history of previous delivery or pregnancy complications.

All data were collected from hospital births, with the exception of Pune and Imesi where home births were also included. As the proportion of home births was small in Europe and Jamaica, samples obtained were likely to have been fairly representative of babies born in these areas. However, in the developing countries, particularly India and China,

proportions of home births were high. Hence mothers included in these samples may have been at higher risk of pregnancy or delivery problems.
The European women were considered to be representative of the whole range of social classes for each dataset. However, in Beijing, the women were typically from a higher social class than average for the city, and in the remaining datasets women tended to be from the middle and lower classes within each population.

Year of birth ranged from 1907 (Sheffield) to 1998 (India, Africa). Secular trends in height and to a lesser extent weight have been demonstrated over the last century (Cole 2000). These were stronger in adults, but also seen at birth, and were probably due to increasing affluence. Hence the validity of comparisons between datasets obtained many years apart may be affected, although within datasets, year of birth effects were generally small.

Non-random missing data may also have introduced some bias. In Aberdeen, Helsinki and Mysore 1, only those subjects who were traced in later life were included in any analysis, and obviously only those traced in later life were included in all the blood pressure analysis. There may have been differences between these groups and those that were not traced, for example, it was likely to have been the healthier babies that survived to childhood or adulthood, so mean anthropometric measurements may have been overestimated. In addition, missing gestational data resulted in exclusion of a number of subjects, particularly in the retrospective datasets. Mothers who knew their LMP were likely to have been more motivated or had previous complications, as mentioned above.

9.3.2 Comparability of measurements

There may be difficulties with comparing anthropometric measurements across datasets, due to use of different equipment and techniques, and also differences in the degree of accuracy in recording. Datasets based on prospectively collected data within research studies rather than obstetric records are likely to have contained more detailed measurements that were recorded more accurately than those based on obstetric records. Difficulties encountered with specific measurements were outlined in §2.4.1 for neonates and §2.4.2 for mothers. In addition, problems with comparing blood pressure measurements of the subject in childhood or adulthood were discussed in §2.4.5. As blood pressure is strongly related to age (Pickering 1972), and the age range both within

and between datasets was so variable, age and sex specific standard deviation scores were used for all analyses, rather than absolute values. A single population had to be used for standardisation to ensure datasets were comparable, although this had the disadvantage of assuming relationships between age and blood pressure were the same in all populations. Although the US population used for standardisation was the most appropriate, it was still not ideal as adult values were only given in five-year age bands rather than one-year, and the data had not been updated since the 1970's, although there is no evidence for secular trends in blood pressure levels.

Maternal and paternal height, and also maternal birthweight were self-reported in some of the studies. Height has been shown to be reported with acceptable accuracy in several studies. For example, Spencer et al. (2002) found correlations of at least 0.9 between self-reported and measured height in a group of men and women aged 35-76 in their Oxford study. Godfrey et al. (1996b) compared recalled maternal birthweight with the actual weight recorded in the original obstetric records for 136 of the mothers from the Southampton 1 dataset who were born in local hospitals. Actual birthweight was on average 32g heavier than recalled birthweight with SD 264g, and 84% differed by 250g or less. Relationships between actual maternal birthweight and neonatal placental and birthweights were found to be similar to those with recalled birthweight. The attenuation of a regression coefficient based on recalled values compared to actual values could be calculated, based on statistical theory. For example, in the Southampton 1 dataset, the 27g increase in neonatal birthweight for every 100g increase in maternal birthweight using the recalled values would become 36g if actual values were used instead, i.e. a relatively small increase.

When analysing relationships between measurements, the only potential confounders adjusted for were neonatal sex and gestational duration, maternal age and parity for mother to baby relationships, and subject's current height, BMI and room temperature for relationships with later blood pressure. There are many other factors that may have had an effect on these relationships, although these were not possible to adjust for due to incomplete information in some datasets, or different methods of measurement across datasets. These include social class, maternal nutrition, smoking and alcohol intake and seasonality amongst others. Hence it is possible that differences in the distribution of these factors across datasets may account for some of the geographical variation seen in phenotypes and anthropometric relationships.

9.3.3 Statistical Methods

A major difficulty when interpreting results was the varying numbers of subjects in each dataset. Where possible, effect sizes rather than p-values were used for interpretation, for example correlation coefficients were colour coded for size rather than significance. In analyses where p-values were used, it may be argued that adjustment should have been made for multiple testing, such as application of Bonferroni corrections. This has not been done because for many of the analyses, knowledge of the relevant literature allowed some pre-conceived ideas of likely results. Also, Bonferroni corrections are very conservative so important results may have been missed, and interpretations of findings depend on the number of tests performed which is extremely subjective. When comparing mother to baby relationships across populations, there were further problems with use of p-values as not all measurements were recorded in all datasets, so the numbers on which the p-values were based varied across each maternal-neonatal pair. For measurements that were recorded in only a small number of datasets, the ability to distinguish between the regression slopes for different datasets was limited. However, interpretation of results was based on graphical representations in addition to p-values, so interesting differences in relationships that were missed by the p-values would still have been identified.

All results were based on cross-sectional data. As anthropometric measurements at birth only summarise fetal growth to a limited extent, it would have been preferable to use longitudinal measurements throughout gestation, but these data did not exist for most of the populations studied. Another potential problem was that some of the datasets included siblings, so not all mother-baby pairs were independent. There were generally very few siblings who tended to be in the larger datasets, although in Beijing 21% of the subjects had siblings also in the dataset. In this dataset, the regression coefficients for mother to baby relationships were compared with those derived from multi-level models which are designed to account for dependence between siblings. Results were very similar, for example, for every kilo increase in maternal weight, neonatal birthweight increased by 20.7(1.4)g without accounting for sibling dependence, and 20.8(1.5)g after accounting for the dependence, adjusting for sex and gestation. Hence it was decided that introducing another level of complexity to the analysis was not worthwhile. Also, if multi-level modelling had been used for all analyses, datasets where the mother's date of birth had not been recorded (Preston, Sheffield, Helsinki), which was required to identify possible siblings, would have had to be excluded.

Hence due to the many difficulties encountered, particularly with comparability across datasets, generalising results based on mean or median values from datasets to populations was limited. However, for characterisation of neonatal, maternal and paternal phenotypes using star graphs and principal component analysis, consistent patterns were generally seen within countries and continents, and across the sexes, parity and maternal age groups. WHO data, based on a common protocol, also provided support where possible, so findings could be presented with confidence. In addition, analyses of associations between variables (mother to baby, father to baby and baby/mother to later blood pressure) were based on relationships between measurements within datasets (correlation and regression coefficients), so many of the issues were less problematic for these.

9.4 Implications and future work

All the measures of maternal size and body composition were independently related to neonatal phenotype and were shown to explain a large part of the geographical variation between neonates, implying that nutrition during the whole of the mother's life cycle is important for fetal growth. For example, the effect of an increase the size of the IQR on neonatal birthweight ranged from 25 to 230g across maternal measures and datasets. These effects were comparable to those seen for other maternal factors, for example neonates born to mothers who smoked are 100 to 300g lighter than those born to mothers who did not smoke (Fisk and Smith 2001). It may be argued that an IQR change is large and hence unobtainable, for example, IQRs for height were 7 to 10cm across the datasets. However secular trends have been demonstrated, for example Sachdev (1997) reviewed a number of studies, many of which showed positive height trends; in one study an increase of 5cm was observed between generations. Any changes can only be expected to come slowly, and even a 100g change in birthweight is clinically important.

This thesis has contributed to the debate on some of the factors that influence neonatal growth. These can be summarised as factors that operate at five different stages:

- Mother's own early life

Maternal birthweight, a reflection of her own intra-uterine environment was the strongest predictor of almost all the neonatal outcomes (Figure 6.24), although was only recorded in two of the datasets. Maternal head, which is indicative of her infant growth and had rarely been investigated before, was shown to influence the growth of her fetus in datasets where

it was available (Figure 6.18). Maternal height, a reflection of her childhood growth was shown to be more important than previously thought in most datasets (Figure 6.16).

- Mother's adult life before pregnancy

Maternal pre-pregnancy measures were available in a small number of the datasets. Although not analysed in detail, maternal BMI, muscle (measured by AMA) and fat (measured by triceps skinfold) had important effects on the neonatal measures that were similar to those of measures recorded at 30-weeks gestation (comment, end §6.3.1).

- Pregnancy

Ideally, factors that operate on fetal growth during pregnancy should be considered separately for each of the three trimesters. However, the data available from this study were not sufficient to draw such conclusions as only the 30-week values were analysed in detail. At this timepoint, maternal BMI had strong effects on neonatal phenotype, particularly in Mysore 2 (Figure 6.16). Maternal fat tended to have a stronger effect than muscle on the neonatal measures especially in Mysore 2, although the effects were reversed in Kasaji, Congo (Figure 6.19). Both the 20-week and 37-week values, where available had similar effects on the neonatal measures as those recorded at 30-weeks gestation (comment, end §6.3.1).

- Paternal size and body composition

Paternal size was also related to neonatal phenotype where measurements were available, independently of maternal size. This indicated genetic effects that appeared to be stronger for the skeleton (measured by height) than the soft tissues (measured by BMI). However, maternal size was more strongly related to the neonatal measures than paternal size (Figure 7.14).

- Placenta

Placental weight influences neonatal outcomes, and correlations of between 0.30 and 0.52 were seen with birthweight across the datasets (Appendix 2b).

However, it is too early to make recommendations for specific countries as not enough is known about optimal neonatal body composition with regard to adult disease. Although there is a large literature on relationships between birthweight and disease in later life, less is known about other body proportions such as length, head, and placental weight. Effects

of neonatal muscle and true measures of adiposity (as opposed to PI, which has been shown to be inadequate) have not been considered. Also, most studies have been undertaken in developed countries, and this thesis has demonstrated that there are large geographical differences in neonatal phenotypes. Hence studies of the effects of neonatal body proportions on disease in later life, particularly in developing countries are required. In addition, short-term outcomes such as infant mortality, as well as disease in later life must also be considered when making recommendations for optimal neonatal body composition. Again, the literature is sparse when considering effects of neonatal anthropometric measures other than birthweight on short-term outcomes.

Further detailed studies of mother to baby relationships are also required. The results from this thesis have added to the body of literature in an area that is currently small, but for relationships other than maternal height and BMI, these have been based only on a small number of datasets; maternal head circumference was only recorded in the UK and India as was maternal birthweight, and measures of maternal muscle and fat were only available in the UK, India, Congo and Jamaica. It would be preferable for maternal measurements to be made before pregnancy, although as near to the time of conception as possible. Similarly, more detailed studies of father to baby relationships are required. While the results of this thesis have added to the sparse literature in this area, it was only possible to consider effects of paternal height in the UK, India and Africa, and paternal BMI in India and Africa. For both mother-baby and father-baby studies, it is vital that data on gestation is collected, as well as other possible confounders such as social class, and that they are undertaken in both developed and developing countries. Regarding the measurements themselves, the possible inadequacies of anthropometry, particularly the fat and muscle values have been discussed, so alternative methods such as bioimpedence, isotope dilution and dual x-ray absorptiometry (DXA) should be considered.

In conclusion, this study has been worthwhile for a number of reasons. It has demonstrated the importance of different aspects of maternal body composition for fetal growth, and highlighted the weaknesses of the current data available, which will enable appropriate data to be collected in the future. The set of statistical methods used can be applied to future data, and the results used to help guide policy on recommendations regarding the ideal maternal body composition for pregnancy once optimal neonatal body composition for adult disease, which may vary across populations, has been established.

Appendices

Appendix 1 Data collection form – placental weighing study

HOSPITAL NUMBER

MOTHER'S SURNAME

MOTHER'S DATE OF BIRTH

DATE OF DELIVERY

TIME OF DELIVERY

LABOUR

- Spontaneous ☐
- Elective caesarean section ☐
- Induced ☐
- Augmented ☐

TYPE OF DELIVERY

- Normal vaginal ☐
- Instrumental ☐
- Elective caesarean section ☐
- Emergency caesarean section ☐

PRESENTATION AT DELIVERY

- Vertex/cephalic ☐
- Breech ☐
- Other ☐

DURATION OF LABOUR

- 1st _____ hrs _____ mins
- 2nd _____ hrs _____ mins
- 3rd _____ hrs _____ mins

PLACENTAL DELIVERY

- Spontaneous expulsion ☐
- Controlled cord traction ☐
- Manual ☐

MEMBRANES

- Complete ☐
- Incomplete ☐
- Doubtful ☐

INFANT SEX

Male ☐ Female ☐

BIRTHWEIGHT

_____ g

ESTIMATED GESTATIONAL AGE

____ weeks ____ days

KNOWN DIABETIC

Yes ☐ No ☐

PLACENTA WEIGHED BY

TIME OF PLACENTAL WEIGHT

PLACENTAL WEIGHT

- Before trimming _____ g
- After cord removed _____ g
- After membranes removed _____ g

Appendix 2 Characterisation of neonatal phenotypes

Appendix 2a Mean/median gestation adjusted neonatal measurements

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Southampton 1	Mean	**3413**	**532**	**50.10**	**33.28**	**16.82**	**35.08**		**33.62**	**11.64**				**27.06**	**70.06**	**104.49**	**15.64**
	SD	444	120	1.84	1.39	0.89	1.21		1.64	0.90				2.11	2.10	4.14	2.84
	N	557	541	541	543	540	547		547	547				541	541	547	541
Southampton 2	Mean	**3423**	**563**	**49.78**	**33.22**	**16.55**	**34.94**		**33.35**	**11.55**				**27.70**	**70.24**	**104.9**	**16.53**
	SD	420	127	1.80	1.32	0.82	1.15		1.51	0.81				2.15	2.19	3.98	3.21
	N	521	506	502	501	501	508		508	508				502	502	508	506
Southampton 3	Mean	**3472**	**518**	**49.71**			**35.19**		**33.54**	**11.49**			**4.80**	**28.15**	**70.86**	**105.04**	**14.97**
	SD	452	108	1.81			1.20		1.65	0.93			1.13	2.34	2.22	4.30	2.45
	N	377	338	373			377		377	377			377	373	373	377	338
Southampton 4	Mean	**3568**	**529**	**50.54**	**34.04**	**16.50**	**35.25**		**34.37**	**11.48**				**27.48**	**69.76**	**102.75**	**14.90**
	SD	434	107	2.03	1.37	1.49	1.18		1.66	0.88				2.41	2.30	4.30	2.48
	N	102	99	100	100	100	102		102	102				100	100	102	99
Preston	Mean	**3179**	**486**	**51.62**			**34.71**							**23.16**	**67.33**		**15.39**
	SD	430	109	2.40			1.66							3.03	3.68		3.12
	N	1014	1014	1013			1014							1013	1013		1014
Sheffield	Mean	**3294**	**502**	**51.20**			**34.67**		**32.97**					**24.61**	**67.83**	**104.81**	**15.37**
	SD	465	108	2.66			1.66		1.93					3.84	3.62	4.35	2.88
	N	4417	3644	4097			4351		2738					4096	4031	2738	3643
Farnborough	Mean	**3322**	**506**	**50.70**			**34.62**							**25.72**	**68.42**		**15.28**
	SD	430	104	2.63			1.36							3.48	3.73		2.66
	N	1677	1649	1535			1543							1535	1535		1649

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	G	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Isle of Man	Mean	**3372**	**493**	**50.06**			**34.66**		**32.50**					**26.75**	**69.28**	**106.86**	**14.64**
	SD	447	101	1.84			1.19		1.58					2.42	2.11	4.19	2.47
	N	387	386	388			388		388					387	388	388	385
Aberdeen	Mean	**3224**	**529**														**14.50**
	SD	416	101														3.29
	N	233	230														230
Helsinki	Mean	**3436**	**515**	**50.19**			**34.74**							**27.07**	**69.25**		**15.05**
	SD	458	100	1.67			1.28							2.38	2.30		2.42
	N	5989	5979	5963			5972							5963	5946		5979
Mysore 1	Mean	**2877**		**48.46**			**34.14**							**25.63**	**70.71**		
	SD	426		3.03			1.70							4.84	4.85		
	N	1236		1180			1172							1180	1168		
Mysore 2	Mean	**2958**	**419**	**49.14**	**32.23**	**16.93**	**34.06**		**32.23**	**10.44**	**22.73**	**4.28**	**4.54**	**24.89**	**69.36**	**104.85**	**14.23**
	SD	413	86	2.08	1.68	1.44	1.28		1.65	0.92	1.86	0.92	0.94	2.61	2.75	5.33	2.31
	N	597	587	595	595	593	597		595	595	595	595	595	595	595	595	587
Pune 1	Mean	**2731**	**364**	**48.15**			**33.34**	**31.45**	**29.84**	**9.82**	**21.18**	**4.28**	**4.23**	**24.45**	**69.31**	**112.05**	**13.37**
	SD	334	76	1.81			1.13	1.57	1.81	0.84	1.91	0.84	0.84	2.28	2.43	6.10	2.26
	N	633	584197	625			628	628	628	628	628	628	627	625	625	628	587
Pune 2	Mean	**2840**	**96**	**47.78**			**33.34**	**31.78**	**29.84**	**9.82**	**21.15**	**4.31**	**4.15**	**26.11**	**69.85**	**112.20**	**14.81**
	SD	392		2.09			1.33	1.93	2.36	0.83	1.82	0.78	0.71	3.29	3.30	7.4	2.83
	N	265	170	230			230	230	230	230	230	230	230	230	230	230	166

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Kandy,Sri Lanka	Mean	**2761**		**48.23**			**33.55**							**23.37**	**69.37**		
	SD	459		2.27			1.22							2.03	2.57		
	N	455		185			98							185	96		
Beijing	Mean	**3156**	**431**	**49.49**	**33.62**	**15.87**	**32.03**							**25.96**	**64.76**		**13.69**
	SD	394	76	1.91	1.57	1.42	1.52							2.14	2.92		1.91
	N	2431	2357	2419	2414	2405	2423							2418	2412		2356
Kasaji,Congo	Mean	**2842**	**382**	**47.84**			**34.08**	**29.69**		**9.58**	**20.96**	**3.79**	**3.81**	**25.82**	**71.03**		**13.54**
	SD	394	77	1.86			1.15	1.78		0.78	1.58	0.84	0.89	2.35	2.48		2.35
	N	338	310	335			334	180		335	331	331	331	335	334		310
Imesi,Nigeria	Mean	**2904**	**468**	**47.81**			**34.01**	**33.09**						**26.69**	**71.26**		**16.38**
	SD	397	98	2.28			1.51	1.86						2.60	2.97		2.87
	N	248	147	254			244	239						243	243		143
Kingston 1	Mean	**3221**	**475**	**49.89**	**33.24**	**16.63**	**34.57**	**32.74**	**32.72**	**10.46**				**26.03**	**69.40**	**105.74**	**14.75**
	SD	438	102	2.57	1.99	1.59	1.36	1.81	1.65	0.93				3.52	3.50	4.54	2.50
	N	490	484	483	480	480	484	478	476	476				483	483	476	484
Kingston 2	Mean	**3159**	**470**	**49.72**	**32.99**	**16.73**	**34.43**							**25.81**	**70.66**		**15.07**
	SD	526	96	3.94	2.99	2.81	2.03							5.33	7.25		2.86
	N	70	70	61	61	61	61							61	61		70

		Birthweight	CH length	Head	Chest	PI	Head/length
		g	cm	cm	cm	kg/m^3	%
WHO Sweden	Median	**3734**	**51.7**	**25.8**	**35.7**	**26.9**	**69.23**
	IQR	3437,3967	50.7,52.7	35.0,36.5	34.6,36.8	25.5,28.2	67.69,70.78
	N	505	503	490	478	503	489
WHO Australia	Median	**3468**	**51.7**	**35.3**	**34.9**	**25.7**	**68.65**
	IQR	3238,3763	50.3,52.8	34.5,36.1	33.8,35.9	24.1,27.1	67.08,70.24
	N	622	598	594	409	598	593
WHO Chile	Median	**3355**	**50.8**	**35.1**	**34.2**	**25.7**	**69.23**
	IQR	3145,3646	49.7,51.9	34.4,35.8	33.3,35.5	24.3,27.2	67.71,70.58
	N	688	688	684	687	688	684
WHO Guatemala	Median	**3256**	**50.1**	**34.8**		**25.8**	**69.49**
	IQR	2949,3550	48.9,51.3	33.9,35.6		24.4,27.4	68.10,70.92
	N	294	294	294		294	294
WHO India	Median	**2995**	**49.8**	**34.4**	**33.1**	**24.1**	**68.75**
	IQR	2828,3269	48.8,51.2	33.7,35.1	32.2,34.1	22.7,26.0	67.21,70.47
	N	504	504	504	504	504	504
WHO China	Median	**3325**	**49.0**	**33.5**	**32.1**	**27.3**	**67.85**
	IQR	3025,3525	47.9,50.1	33.2,34.3	31.2,33.8	25.6,30.5	66.08,69.94
	N	541	541	541	270	540	541
WHO Nigeria	Median	**3078**	**49.9**	**34.9**	**33.1**	**24.8**	**3078**
	IQR	2843,3356	48.7,51.5	33.9,35.9	32.0,34.3	22.8,26.5	2843,3355
	N	512	511	512	512	511	512

Appendix 2b Further principal components analysis

Across datasets	Original variables	PC1 Coefficients*	% variation explained	PC2 Coefficients*	% variation explained
19 datasets	Birthweight	0.54	78	-0.17	12
	CH length	0.48		-0.56	
	Head	0.45		0.81	
	Placental weight	0.52		-0.02	
5 datasets	Birthweight	0.51	69	-0.05	13
	CH length	0.42		-0.43	
	Head	0.44		-0.39	
	MUAC	0.48		0.15	
	Subscapular	0.38		0.80	
Within datasets	Original variables	PC1 Coefficients*	% variation explained	PC2 Coefficients*	% variation explained
Southampton 3	Birthweight	0.53	67	-0.02	15
	CH length	0.43		-0.54	
	Head	0.44		-0.31	
	MUAC	0.46		0.23	
	Subscapular	0.37		0.74	
Mysore 2	Birthweight	0.52	66	-0.05	15
	CH length	0.41		-0.58	
	Head	0.43		-0.35	
	MUAC	0.46		0.31	
	Subscapular	0.40		0.67	
Pune 1	Birthweight	0.52	63	0.01	15
	CH length	0.44		-0.42	
	Head	0.43		-0.31	
	MUAC	0.47		0.04	
	Subscapular	0.36		0.85	
Pune 2	Birthweight	0.52	63	0.04	15
	CH length	0.37		0.74	
	Head	0.43		0.19	
	MUAC	0.48		-0.29	
	Subscapular	0.42		-0.57	
Kasaji, Congo	Birthweight	0.50	70	-0.03	15
	CH length	0.45		-0.39	
	Head	0.42		-0.51	
	MUAC	0.48		0.26	
	Subscapular	0.38		0.73	

*all variable standardised

Appendix 2c Pearson correlations between gestation adjusted neonatal measurements

|r|<0.10 0.10≤|r|≤0.20 |r|>0.20 |r| = absolute correlation

Bwt = birthweight, pwt = placental weight, HL = head to length ratio, HA = head to abdomen ratio

	Southampton 1	Southampton 2	Southampton 3	Southampton 4	Preston	Sheffield	Farnborough	Isle of Man	Aberdeen	Helsinki	Mysore 1	Mysore 2	Pune 1	Pune 2	Kandy, Sri Lanka	Beijing	Kasaji, Congo	Imesi, Nigeria	Kingston 1	Kingston 2
Bwt/Pwt	0.57	0.52	0.63	0.54	0.43	0.50	0.54	0.57	0.35	0.58	0.30	0.63	0.60	0.60		0.62	0.54	0.52	0.61	0.43
Bwt/CHL	0.79	0.78	0.77	0.73	0.53	0.56	0.55	0.74		0.75	0.42	0.70	0.69	0.58	0.83	0.76	0.76	0.73	0.57	0.56
Bwt/CRL	0.79	0.79		0.66								0.71				0.65			0.57	0.52
Bwt/Leg length	0.40	0.44		0.39								0.18				0.31			0.21	0.24
Bwt/Head	0.72	0.70	0.71	0.68	0.55	0.52	0.58	0.71		0.66	0.44	0.70	0.63	0.69	0.67	0.53	0.68	0.62	0.60	0.67
Bwt/Chest													0.79	0.72			0.84	0.72	0.79	
Bwt/Abdomen	0.87	0.87	0.87	0.83		0.65		0.82				0.86	0.71	0.66					0.83	
Bwt/MUAC	0.84	0.84	0.80	0.77								0.76	0.70	0.73			0.86		0.73	
Bwt/AMA												0.69	0.57	0.64			0.84			
Bwt/Triceps												0.64	0.57	0.56			0.56			
Bwt/SS			0.63									0.64	0.55	0.62			0.58			
Bwt/PI	0.52	0.49	0.55	0.41	0.48	0.34	0.27	0.57		0.68	0.36	0.51	0.50	0.46	0.48	0.46	0.57	0.38	0.34	0.16
Bwt/HL	-0.14	-0.16	-0.11	-0.21	0.03	-0.08	-0.11	-0.10		-0.03	-0.07	-0.09	-0.14	0.06	-0.37	-0.10	-0.20	-0.13	-0.12	-0.12
Bwt/HA	-0.44	-0.43	-0.45	-0.42		-0.27		-0.40				-0.34	-0.42	-0.37					-0.45	
Bwt/PwtBwt	-0.01	-0.03	0.02	-0.06	-0.21	-0.18	-0.11	-0.11	-0.33	-0.15	-0.44	-0.09	-0.01	-0.05		-0.13	-0.19	-0.13	-0.06	-0.40

	Southampton 1	Southampton 2	Southampton 3	Southampton 4	Preston	Sheffield	Farnborough	Isle of Man	Aberdeen	Helsinki	Mysore 1	Mysore 2	Pune 1	Pune 2	Kandy, Sri Lanka	Beijing	Kasaji, Congo	Imesi, Nigeria	Kingston 1	Kingston 2
Pwt/CHL	0.40	0.40	0.50	0.43	0.15	0.58	0.25	0.36		0.45	0.16	0.44	0.39	0.44		0.49	0.48	0.40	0.40	0.33
Pwt/CRL	0.39	0.41		0.38								0.44				0.42			0.41	0.21
Pwt/Leg length	0.22	0.21		0.27								0.12				0.19			0.10	0.25
Pwt/Head	0.41	0.36	0.52	0.45	0.24	0.24	0.34	0.39		0.41	0.11	0.50	0.39	0.46		0.33	0.40	0.42	0.39	0.35
Pwt/Chest													0.48	0.42			0.52	0.45	0.55	
Pwt/Abdomen	0.49	0.47	0.56	0.46		0.35		0.46				0.59	0.46	0.51					0.58	
Pwt/MUAC	0.43	0.44	0.45	0.37								0.50	0.45	0.49			0.49		0.51	
Pwt/AMA												0.42	0.38	0.42			0.46			
Pwt/Triceps												0.50	0.36	0.39			0.34			
Pwt/SS			0.40									0.47	0.32	0.41			0.36			
Pwt/PI	0.37	0.26	0.32	0.19	0.29	0.15	0.18	0.38		0.37	0.08	0.30	0.33	0.24		0.25	0.24	0.26	0.15	0.01
Pwt/HL	-0.02	-0.08	-0.01	-0.06	0.08	-0.06	0.01	0.01		0.01	-0.08	-0.01	-0.04	-0.00		-0.07	-0.14	0.03	-0.09	-0.11
Pwt/HA	-0.27	-0.24	-0.24	-0.17		-0.17		-0.23				-0.23	-0.27	-0.35					-0.34	
Pwt/PwtBwt	0.81	0.83	0.78	0.81	0.78	0.74	0.77	0.74	0.75	0.71	0.71	0.71	0.78	0.76		0.69	0.71	0.78	0.75	0.64
CHL/CRL	0.89	0.90		0.68								0.73				0.68			0.78	0.70
CHL/Leg length	0.68	0.73		0.74								0.61				0.59			0.63	0.65
CHL/Head	0.65	0.60	0.60	0.60	0.32	0.43	0.31	0.63		0.56	0.28	0.52	0.53	0.39	0.62	0.46	0.68	0.58	0.41	0.62
CHL/Chest													0.65	0.36			0.72	0.59	0.53	
CHL/Abdomen	0.67	0.68	0.64	0.63		0.47		0.60				0.61	0.52	0.26					0.53	
CHL/MUAC	0.58	0.55	0.48	0.52								0.44	0.55	0.40			0.62		0.42	
CHL/AMA												0.42	0.50	0.33			0.59			
CHL/Triceps												0.32	0.31	0.35			0.44			
CHL/SS			0.31									0.35	0.28	0.32			0.41			
CHL/PI	-0.10	-0.15	-0.11	-0.32	-0.48	-0.52	-0.64	-0.12		0.03	-0.68	-0.24	-0.27	-0.46	-0.07	-0.22	-0.09	-0.35	-0.56	-0.70
CHL/HL	-0.49	-0.52	-0.50	-0.60	-0.56	-0.58	-0.73	-0.49		-0.39	-0.71	-0.58	-0.56	-0.61	-0.63	-0.38	-0.48	-0.50	-0.70	-0.45
CHL/HA	-0.27	-0.29	-0.27	-0.24		-0.14		-0.20				-0.22	-0.27	-0.09					-0.25	
CHL/PwtBwt	-0.07	-0.03	0.05	-0.01	-0.20	-0.10	-0.10	-0.17		-0.09	-0.14	-0.06	-0.02	0.06		-0.08	-0.08	-0.10	0.02	-0.23

	Southampton 1	Southampton 2	Southampton 3	Southampton 4	Preston	Sheffield	Farnborough	Isle of Man	Aberdeen	Helsinki	Mysore 1	Mysore 2	Pune 1	Pune 2	Kandy, Sri Lanka	Beijing	Kasaji, Congo	Imesi, Nigeria	Kingston 1	Kingston 2
CRL/Leg length	0.27	0.36		0.00								-0.10				-0.18			0.01	-0.08
CRL/Head	0.62	0.58		0.52								0.56				0.43			0.41	0.84
CRL/Chest																			0.54	
CRL/Abdomen	0.66	0.67		0.63								0.59							0.54	
CRL/MUAC	0.61	0.60		0.55								0.52							0.46	
CRL/AMA												0.48								
CRL/Triceps												0.40								
CRL/SS												0.38								
CRL/PI	0.05	-0.02		0.02								0.14				0.05			-0.31	-0.35
CRL/HL	-0.38	-0.44		-0.30								-0.23				-0.14			-0.51	-0.10
CRL/HA	-0.27	-0.30		-0.30								-0.17							-0.29	
CRL/PwtBwt	-0.08	-0.02		-0.01								-0.08				-0.06			0.05	-0.27
Leg length/Head	0.37	0.37		0.34								0.09				0.15			0.17	-0.01
Leg length/Chest																			0.20	
Leg length/Abdo	0.36	0.40		0.28								0.18							0.19	
Leg length/MUAC	0.25	0.24		0.20								0.02							0.10	
Leg length/AMA												0.04								
Leg length/Triceps												-0.01								
Leg length/SS												0.05								
Leg length/PI	-0.30	-0.31		-0.45								-0.51				-0.34			-0.51	-0.60
Leg length/HL	-0.42	-0.44		-0.54								-0.58				-0.35			-0.54	-0.53
Leg length/HA	-0.12	-0.16		-0.05								-0.12							-0.06	
Leg length/PwtBwt	-0.03	-0.03		-0.01								0.00				-0.04			-0.04	-0.02

	Southampton 1	Southampton 2	Southampton 3	Southampton 4	Preston	Sheffield	Farnborough	Isle of Man	Aberdeen	Helsinki	Mysore 1	Mysore 2	Pune 1	Pune 2	Kandy, Sri Lanka	Beijing	Kasaji, Congo	Imesi, Nigeria	Kingston 1	Kingston 2
Head/Chest													0.61	0.58			0.60	0.63	0.54	
Head/Abdo	0.59	0.57	0.56	0.53		0.72		0.60				0.64	0.50	0.55					0.56	
Head/MUAC	0.56	0.55	0.56	0.46								0.56	0.53	0.55			0.57		0.46	
Head/AMA												0.50	0.48	0.52			0.57			
Head/Triceps												0.46	0.31	0.30			0.35			
Head/SS			0.40									0.38	0.32	0.36			0.35			
Head/PI	0.28	0.27	0.33	0.14	0.24	0.07	0.18	0.29		0.38	0.07	0.34	0.20	0.34	0.17	0.17	0.21	0.15	0.14	-0.13
Head/HL	0.35	0.37	0.39	0.27	0.60	0.49	0.42	0.37		0.55	0.47	0.39	0.40	0.50	0.19	0.65	0.18	0.41	0.36	0.06
Head/HA	0.14	0.19	0.16	0.19		0.12		0.12				0.12	0.06	-0.07					0.20	
Head/PwtBwt	-0.03	-0.03	0.08	0.07	-0.11	-0.12	-0.01	-0.10		-0.06	-0.20	0.01	0.02	0.01		-0.06	-0.11	-0.01	-0.01	-0.25
Chest/Abdo													0.74	0.74					0.86	
Chest/MUAC													0.76	0.66			0.82		0.67	
Chest/AMA													0.68	0.61			0.78			
Chest/Triceps													0.43	0.40			0.60			
Chest/SS													0.45	0.57			0.56			
Chest/PI													0.28	0.41			0.39	0.27	0.18	
Chest/HL													-0.11	0.17			-0.23	0.00	-0.15	
Chest/HA													-0.46	-0.54					-0.55	
Chest/PwtBwt													0.01	-0.09			-0.08	-0.06	0.05	
Abdo/MUAC	0.80	0.78	0.75	0.71								0.68	0.66	0.63					0.69	
Abdo/AMA												0.62	0.56	0.62						
Abdo/Triceps												0.56	0.49	0.29						
Abdo/SS			0.56									0.59	0.48	0.53						
Abdo/PI	0.49	0.43	0.52	0.33		0.17		0.48				0.43	0.33	0.44					0.22	
Abdo/HL	-0.14	-0.18	-0.14	-0.24		0.20		-0.05				-0.06	-0.08	0.24					-0.13	
Abdo/HA	-0.72	-0.70	-0.72	-0.73		-0.60		-0.72				-0.54	-0.83	-0.86					-0.70	
Abdo/PwtBwt	-0.01	-0.00	0.03	-0.04		-0.13		-0.10				-0.02	0.05	0.04					0.06	

	Southampton 1	Southampton 2	Southampton 3	Southampton 4	Preston	Sheffield	Farnborough	Isle of Man	Aberdeen	Helsinki	Mysore 1	Mysore 2	Pune 1	Pune 2	Kandy, Sri Lanka	Beijing	Kasaji, Congo	Imesi, Nigeria	Kingston 1	Kingston 2
MUAC/AMA												0.96	0.95	0.96			0.95			
MUAC/Triceps												0.69	0.44	0.52			0.68			
MUAC/SS			0.53									0.61	0.47	0.61			0.68			
MUAC/PI	0.57	0.56	0.63	0.37								0.51	0.27	0.37			0.55		0.25	
MUAC/HL	-0.08	-0.05	0.05	-0.17								0.05	-0.07	0.11			-0.14		-0.09	
MUAC/HA	-0.51	-0.45	-0.44	-0.45								-0.27	-0.42	-0.43					-0.42	
MUAC/PwtBwt	-0.06	-0.01	-0.05	-0.09								-0.06	0.05	0.04			-0.15		0.05	
AMA/Triceps												0.46	0.14	0.26			0.42			
AMA/SS												0.45	0.23	0.47			0.48			
AMA/PI												0.45	0.17	0.34			0.55			
AMA/HL												0.03	-0.06	0.14			-0.14			
AMA/HA												-0.25	-0.33	-0.43						
AMA/PwtBwt												-0.09	0.05	0.04			-0.16			
Triceps/SS												0.77	0.80	0.64			0.85			
Triceps/PI												0.48	0.38	0.24			0.31			
Triceps/HL												0.09	-0.04	-0.07			-0.14			
Triceps/HA												-0.24	-0.37	-0.17						
Triceps/PwtBwt												0.06	0.03	0.04			-0.08			
SS/PI			0.56									0.44	0.39	0.34			0.37			
SS/HL			0.07									-0.01	0.00	0.02			-0.10			
SS/HA			-0.34									-0.33	-0.35	-0.42						
SS/PwtBwt			0.03									0.02	0.01	-0.01			-0.06			
PI/HL	0.45	0.47	0.48	0.52	0.62	0.57	0.74	0.47		0.39	0.68	0.59	0.49	0.73	0.39	0.36	0.31	0.50	0.69	0.45
PI/HA	-0.36	-0.28	-0.35	-0.27		-0.13		-0.35				-0.19	-0.25	-0.32					-0.15	
PI/PwtBwt	0.09	-0.01	-0.02	-0.04	-0.01	-0.07	0.02	0.02		-0.13	-0.20	-0.07	0.03	-0.14		-0.10	-0.20	-0.07	-0.10	-0.09
HL/HA	0.48	0.54	0.49	0.49		0.26		0.38				0.37	0.35	0.02					0.41	
HL/PwtBwt	0.07	0.00	0.04	0.10	0.08	0.00	0.09	0.08		0.04		0.07	0.04	-0.06		-0.00	-0.01	0.08	-0.02	0.04
HA/PwtBwt	-0.01	-0.03	0.03	0.11		0.03		0.02				0.01	-0.04	-0.03					-0.07	

Appendix 2d Mean gestation adjusted neonatal measurements by sex with t-tests for differences

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Southampton 1	Boys	**3496**	**541**	**50.62**	**33.64**	**16.98**	**35.43**		**33.78**	**11.72**				**26.85**	**70.03**	**105.02**	**15.48**
	Girls	**3318**	**522**	**49.51**	**32.88**	**16.63**	**34.69**		**33.44**	**11.55**				**27.29**	**70.09**	**103.90**	**15.82**
	p	<0.001	0.06	<0.001	<0.001	<0.001	<0.001		0.02	0.02				0.02	0.7	0.001	0.2
Southampton 2	Boys	**3482**	**571**	**50.32**	**33.56**	**16.76**	**35.30**		**33.47**	**11.58**				**27.30**	**70.21**	**105.64**	**16.43**
	Girls	**3363**	**555**	**49.24**	**32.89**	**16.35**	**34.57**		**33.22**	**11.51**				**28.09**	**70.26**	**104.20**	**16.63**
	p	0.001	0.02	<0.001	<0.001	<0.001	<0.001		0.07	0.3				<0.001	0.8	<0.001	0.5
Southampton 3	Boys	**3543**	**533**	**50.08**			**35.51**		**33.75**	**11.55**			**4.72**	**28.08**	**70.96**	**105.36**	**15.04**
	Girls	**3400**	**503**	**49.33**			**34.87**		**33.33**	**11.42**			**4.89**	**28.22**	**70.75**	**104.73**	**14.89**
	p	0.002	0.01	<0.001			<0.001		0.01	0.2			0.1	0.6	0.4	0.2	0.6
Southampton 4	Boys	**3616**	**538**	**51.05**	**34.22**	**16.83**	**35.66**		**34.51**	**11.51**				**27.06**	**69.86**	**103.5**	**14.87**
	Girls	**3529**	**520**	**50.12**	**33.90**	**16.22**	**34.91**		**34.25**	**11.45**				**27.83**	**69.68**	**102.1**	**14.92**
	p	0.3	0.4	0.02	0.2	0.04	0.001		0.4	0.7				0.1	0.7	0.1	0.9
Preston	Boys	**3231**	**490**	**51.90**			**34.90**							**23.18**	**67.35**		**15.25**
	Girls	**3128**	**483**	**51.35**			**34.52**							**23.14**	**67.31**		**15.54**
	p	<0.001	0.3	<0.001			<0.001							0.8	0.9		0.2
Sheffield	Boys	**3359**	**503**	**51.49**			**34.97**		**33.15**					**24.67**	**68.1**	**105.2**	**15.1**
	Girls	**3225**	**502**	**50.90**			**34.34**		**32.76**					**24.55**	**67.6**	**104.4**	**15.7**
	p	<0.001	0.8	<0.001			<0.001		<0.001					0.3	<0.001	<0.001	<0.001
Farnborough	Boys	**3392**	**515**	**51.05**			**34.90**							**25.76**	**68.51**		**15.23**
	Girls	**3245**	**496**	**50.34**			**34.32**							**25.67**	**68.33**		**15.34**
	p	<0.001	<0.001	<0.001			<0.001							0.6	0.3		0.4
Isle of Man	Boys	**3439**	**498**	**50.49**			**34.96**		**32.73**					**26.62**	**69.28**	**106.99**	**14.43**
	Girls	**3306**	**488**	**49.63**			**34.36**		**32.28**					**26.89**	**69.28**	**106.73**	**14.85**
	p	0.003	0.3	<0.001			<0.001		0.005					0.3	0.99	0.6	0.1

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Aberdeen	Boys	**3277**	**518**														**15.88**
	Girls	**3175**	**539**														**17.10**
	p	0.06	0.1														0.005
Helsinki	Boys	**3507**	**518**	**50.49**			**35.06**							**27.14**	**69.47**		**14.81**
	Girls	**3362**	**513**	**49.88**			**34.40**							**27.00**	**69.01**		**15.30**
	p	<0.001	0.06	<0.001			<0.001							0.02	<0.001		<0.001
Mysore 1	Boys	**2949**		**48.80**			**34.38**							**25.71**	**70.74**		
	Girls	**2797**		**48.08**			**33.88**							**25.53**	**70.69**		
	p	<0.001		<0.001			<0.001							0.5	0.9		
Mysore 2	Boys	**3010**	**419**	**49.48**	**32.48**	**17.01**	**34.35**		**32.30**	**10.51**	**22.94**	**4.21**	**4.45**	**24.82**	**69.44**	**106.32**	**13.99**
	Girls	**2908**	**420**	**48.82**	**32.00**	**16.85**	**33.78**		**32.16**	**10.38**	**22.53**	**4.35**	**4.63**	**24.96**	**6.927**	**103.46**	**14.45**
	p	0.002	0.9	<0.001	<0.001	0.2	<0.001		0.3	0.08	0.008	0.07	0.02	0.5	0.5	<0.001	0.02
Pune 1	Boys	**2786**	**369**	**48.49**			**33.64**	**31.63**	**29.86**	**9.84**	**21.28**	**4.24**	**4.16**	**24.45**	**69.43**	**112.96**	**13.25**
	Girls	**2668**	**358**	**47.74**			**33.00**	**31.24**	**29.81**	**9.80**	**21.07**	**4.32**	**4.32**	**24.45**	**69.17**	**111.01**	**13.51**
	p	<0.001	0.1	<0.001			<0.001	0.002	0.7	0.5	0.2	0.2	0.02	0.997	0.2	<0.001	0.2
Pune 2	Boys	**2877**	**409**	**47.98**			**33.64**	**31.78**	**29.65**	**9.89**	**21.34**	**4.27**	**4.10**	**26.08**	**70.18**	**113.94**	**14.29**
	Girls	**2803**	**429**	**47.58**			**33.03**	**31.79**	**30.03**	**9.75**	**20.95**	**4.36**	**4.20**	**26.15**	**69.51**	**110.43**	**15.34**
	p	0.1	0.2	0.1			<0.001	0.96	0.2	0.2	0.1	0.4	0.3	0.9	0.1	<0.001	0.02
Kandy,Sri Lanka	Boys	**2797**		**48.79**			**34.00**							**23.03**	**69.39**		
	Girls	**2723**		**47.74**			**33.15**							**23.67**	**69.34**		
	p	0.09		0.001			<0.001							0.03	0.9		
Beijing	Boys	**3228**	**438**	**49.92**	**33.88**	**16.03**	**32.29**							**25.88**	**64.72**		**13.59**
	Girls	**3087**	**424**	**49.09**	**33.38**	**15.71**	**31.78**							**23.03**	**64.80**		**13.77**
	p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001							0.08	0.5		0.02

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Kasaji,Congo	Boys	**2846**	**375**	**48.08**			**34.27**	**29.63**		**9.50**	**20.91**	**3.63**	**3.60**	**25.43**	**70.83**		**13.31**
	Girls	**2838**	**389**	**47.58**			**33.88**	**29.76**		**9.67**	**21.02**	**3.97**	**4.05**	**26.24**	**71.26**		**13.79**
	p	0.9	0.1	0.01			0.002	0.6		0.04	0.5	<0.001	<0.001	0.002	0.1		0.08
Imesi,Nigeria	Boys	**2962**	**479**	**48.20**			**34.38**	**33.34**						**26.64**	**71.46**		**16.44**
	Girls	**2859**	**460**	**47.49**			**33.71**	**32.89**						**26.72**	**71.11**		**16.33**
	p	0.04	0.2	0.02			<0.001	0.06						0.98	0.4		0.8
Kingston 1	Boys	**3323**	**486**	**50.54**	**33.59**	**16.93**	**35.00**	**33.08**	**33.05**	**10.58**				**25.85**	**69.37**	**105.88**	**14.60**
	Girls	**3139**	**466**	**49.36**	**32.95**	**16.40**	**34.21**	**32.46**	**32.45**	**10.37**				**26.17**	**69.43**	**105.63**	**14.88**
	p	<0.001	0.03	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.01				0.3	0.8	0.6	0.2
Kingston 2	Boys	**3358**	**484**	**50.38**	**33.65**	**16.73**	**34.86**							**26.66**	**69.49**		**14.58**
	Girls	**2948**	**455**	**49.03**	**32.31**	**16.73**	**33.99**							**24.92**	**71.88**		**15.58**
	p	0.001	0.2	0.2	0.08	0.995	0.1							0.2	0.2		0.1

Appendix 2e Sex differences in lengths of rays for star graphs

Males - females	Birthweight	CH length	Head
Southampton 1	0.16	0.21	0.17
Southampton 2	0.10	0.20	0.16
Southampton 3	0.13	0.14	0.14
Southampton 4	0.08	0.18	0.17
Preston	0.09	0.10	0.09
Sheffield	0.12	0.11	0.14
Farnborough	0.13	0.13	0.13
Isle of Man	0.12	0.16	0.14
Helsinki	0.13	0.12	0.15
Mysore 1	0.13	0.14	0.11
Mysore 2	0.09	0.13	0.13
Pune 1	0.10	0.14	0.14
Pune 2	0.06	0.08	0.14
Kandy, Sri Lanka	0.07	0.20	0.19
Beijing	0.12	0.16	0.11
Kasaji, Congo	0.01	0.09	0.09
Imesi, Nigeria	0.09	0.13	0.15
Kingston 1	0.16	0.22	0.18
Kingston 2	0.36	0.26	0.20

Appendix 2f Mean gestation adjusted neonatal measurements by parity group with t-tests for differences

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Southampton 1	Para 0	**3356**	**519**	**49.96**	**33.22**	**16.74**	**35.01**		**33.39**	**11.52**				**26.85**	**70.11**	**104.99**	**15.48**
	Para 1+	**3476**	**547**	**50.26**	**33.36**	**16.90**	**35.16**		**33.88**	**11.78**				**27.28**	**70.00**	**103.94**	**15.81**
	p	0.001	0.006	0.06	0.2	0.04	0.1		<0.001	0.001				0.02	0.6	0.003	0.2
Southampton 2	Para 0	**3361**	**544**	**49.55**	**33.03**	**16.51**	**34.77**		**33.05**	**11.46**				**27.54**	**70.23**	**105.36**	**16.23**
	Para 1+	**3480**	**581**	**49.99**	**33.40**	**16.59**	**35.09**		**33.62**	**11.63**				**27.84**	**70.24**	**104.53**	**16.81**
	p	0.001	0.001	0.006	0.002	0.3	0.002		<0.001	0.02				0.1	0.9	0.02	0.04
Southampton 3	Para 0	**3402**	**511**	**49.54**			**35.07**		**33.24**	**11.36**			**4.72**	**27.85**	**70.87**	**105.65**	**15.06**
	Para 1+	**3536**	**525**	**49.86**			**35.30**		**33.83**	**11.60**			**4.88**	**28.42**	**70.84**	**104.49**	**14.88**
	p	0.004	0.2	0.08			0.06		<0.001	0.01			0.2	0.02	0.9	0.01	0.5
Southampton 4	Para 0	**3467**	**529**	**50.19**	**33.68**	**16.51**	**35.00**		**33.96**	**11.26**				**27.19**	**69.75**	**103.28**	**15.23**
	Para 1+	**3691**	**529**	**50.96**	**34.48**	**16.48**	**35.56**		**34.86**	**11.75**				**27.84**	**69.78**	**102.11**	**14.45**
	p	0.009	0.997	0.06	0.003	0.9	0.02		0.006	0.005				0.2	0.9	0.2	0.1
Preston	Para 0	**3155**	**485**	**51.46**			**34.68**							**23.21**	**67.50**		**15.47**
	Para 1+	**3284**	**493**	**52.41**			**34.81**							**22.87**	**66.51**		**15.06**
	p	<0.001	0.4	<0.001			0.4							0.2	0.001		0.1
Sheffield	Para 0	**3182**	**486**	**50.94**			**34.53**		**32.68**					**24.16**	**67.90**	**105.27**	**15.36**
	Para 1+	**3366**	**513**	**51.38**			**34.76**		**33.18**					**24.89**	**67.78**	**104.47**	**15.38**
	p	<0.001	<0.001	<0.001			<0.001		<0.001					<0.001	0.3	<0.001	0.8
Farnborough	Para 0	**3274**	**497**	**50.50**			**34.55**							**25.61**	**68.57**		**15.21**
	Para 1+	**3365**	**515**	**50.87**			**34.67**							**25.80**	**68.30**		**15.35**
	p	<0.001	<0.001	0.005			0.08							0.3	0.2		0.3

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Helsinki	Para 0	**3313**	**499**	**49.95**			**34.60**							**26.49**	**69.32**		**15.12**
	Para 1+	**3528**	**528**	**50.37**			**34.84**							**27.50**	**69.19**		**15.01**
	p	<0.001	<0.001	<0.001			<0.001							<0.001	0.04		0.08
Mysore 1	Para 0	**2820**		**48.49**			**34.17**							**25.06**	**70.72**		
	Para 1+	**2914**		**48.45**			**34.13**							**25.96**	**70.70**		
	p	<0.001		0.8			0.7							0.002	0.96		
Mysore 2	Para 0	**2909**	**407**	**49.05**	**32.11**	**16.96**	**33.96**		**32.03**	**10.36**	**22.62**	**4.17**	**4.40**	**24.64**	**69.30**	**105.35**	**14.05**
	Para 1+	**3007**	**432**	**49.24**	**32.35**	**16.89**	**34.16**		**32.42**	**10.52**	**22.84**	**4.40**	**4.69**	**25.14**	**69.41**	**104.34**	**14.41**
	p	0.003	<0.001	0.3	0.08	0.6	0.06		0.004	0.04	0.2	0.002	<0.001	0.02	0.6	0.02	0.06
Pune 1	Para 0	**2625**	**351**	**47.87**			**33.23**	**31.06**	**29.42**	**9.67**	**21.01**	**4.02**	**3.92**	**23.88**	**69.48**	**113.26**	**13.36**
	Para 1+	**2778**	**370**	**48.27**			**33.40**	**31.62**	**30.02**	**9.89**	**21.26**	**4.39**	**4.37**	**24.71**	**69.23**	**111.51**	**13.38**
	p	<0.001	0.005	0.01			0.1	<0.001	<0.001	0.003	0.1	<0.001	<0.001	<0.001	0.2	0.001	0.9
Pune 2	Para 0	**2927**	**436**	**48.19**			**33.59**	**31.90**	**30.09**	**9.91**	**21.34**	**4.35**	**4.24**	**26.39**	**69.79**	**112.20**	**15.01**
	Para 1+	**2824**	**416**	**47.71**			**33.29**	**31.76**	**29.79**	**9.81**	**21.11**	**4.31**	**4.13**	**26.07**	**69.87**	**112.23**	**14.80**
	p	0.1	0.3	0.2			0.2	0.7	0.5	0.5	0.5	0.8	0.4	0.6	0.9	0.98	0.7
Kandy,Sri Lanka	Para 0	**2708**		**47.79**			**33.33**							**23.04**	**69.77**		
	Para 1+	**2809**		**48.64**			**33.80**							**23.67**	**68.91**		
	p	0.02		0.01			0.06							0.04	0.1		
Beijing	Para 0	**3085**	**422**	**49.32**	**33.50**	**15.82**	**31.77**							**25.66**	**64.46**		**13.73**
	Para 1+	**3221**	**440**	**49.65**	**33.73**	**15.91**	**32.26**							**26.24**	**65.03**		**13.65**
	p	<0.001	<0.001	<0.001	<0.001	0.09	<0.001							<0.001	<0.001		0.3
Kasaji,Congo	Para 0	**2632**	**371**	**46.94**			**33.69**	**28.67**		**9.17**	**20.20**	**3.45**	**3.49**	**25.25**	**71.33**		**14.29**
	Para 1+	**2924**	**386**	**48.20**			**34.24**	**30.10**		**9.74**	**21.26**	**3.92**	**3.94**	**26.04**	**70.92**		**13.23**
	p	<0.001	0.1	<0.001			<0.001	<0.001		<0.001	<0.001	<0.001	<0.001	0.006	0.2		<0.001

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Imesi,Nigeria	Para 0	**2892**	**538**	**47.91**			**33.66**	**32.60**						**26.41**	**70.26**		**18.83**
	Para 1+	**2938**	**477**	**47.91**			**34.15**	**33.22**						**26.86**	**71.39**		**16.37**
	p	0.7	0.2	0.999			0.4	0.4						0.6	0.3		0.07
Kingston 1	Para 0	**3160**	**469**	**49.59**	**33.17**	**16.42**	**34.40**	**32.53**	**32.53**	**10.42**				**25.95**	**69.49**	**106.00**	**14.86**
	Para 1+	**3280**	**482**	**50.18**	**33.30**	**16.84**	**34.72**	**32.95**	**32.90**	**10.51**				**26.11**	**69.32**	**105.48**	**14.67**
	p	0.002	0.2	0.01	0.5	0.003	0.009	0.01	0.01	0.3				0.6	0.6	0.2	0.4
Kingston 2	Para 0	**3055**	**460**	**49.54**	**32.88**	**16.67**	**34.12**							**24.78**	**68.95**		**15.30**
	Para 1+	**3290**	**483**	**49.94**	**33.13**	**16.82**	**34.83**							**27.11**	**72.83**		**14.77**
	p	0.06	0.3	0.7	0.7	0.8	0.2							0.09	0.04		0.4

Appendix 2g Parity differences in lengths of rays for star graphs

Para ≥1 - para 0	Birthweight	CH length	Head
Southampton 1	0.10	0.05	0.04
Southampton 2	0.10	0.08	0.07
Southampton 3	0.11	0.06	0.05
Southampton 4	0.18	0.13	0.13
Preston	0.11	0.16	0.03
Sheffield	0.15	0.07	0.05
Farnborough	0.07	0.06	0.03
Helsinki	0.18	0.07	0.05
Mysore 1	0.07	-0.01	-0.002
Mysore 2	0.08	0.03	0.05
Pune 1	0.13	0.07	0.04
Pune 2	-0.08	-0.08	-0.07
Kandy, Sri Lanka	0.08	0.15	0.11
Beijing	0.11	0.06	0.11
Kasaji, Congo	0.24	0.22	0.13
Imesi, Nigeria	0.04	0.0002	0.11
Kingston 1	0.10	0.10	0.08
Kingston 2	0.19	0.07	0.16

Appendix 2h Mean gestation adjusted neonatal measurements by maternal age with analysis of variance for differences

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Southampton 1	<20y	**3374**	**508**	**49.87**	**33.37**	**16.50**	**35.09**		**33.15**	**11.51**				**27.02**	**70.40**	**106.00**	**15.02**
	20-30y	**3416**	**536**	**50.10**	**33.30**	**16.80**	**35.06**		**33.68**	**11.64**				**27.09**	**70.04**	**104.28**	**15.72**
	>30y	**3417**	**530**	**50.20**	**33.19**	**17.02**	**35.14**		**33.63**	**11.69**				**26.97**	**69.99**	**104.64**	**15.60**
	P	0.8	0.3	0.6	0.7	0.003	0.8		0.1	0.5				0.9	0.5	0.03	0.3
Southampton 2	<20y	**3250**	**571**	**49.14**	**32.79**	**16.34**	**34.63**		**32.66**	**11.30**				**27.12**	**70.50**	**106.08**	**17.52**
	20-30y	**3400**	**561**	**49.64**	**33.13**	**16.51**	**34.87**		**33.29**	**11.52**				**27.69**	**70.28**	**104.90**	**16.59**
	>30y	**3501**	**568**	**50.18**	**33.49**	**16.69**	**35.14**		**33.57**	**11.64**				**27.79**	**70.10**	**104.80**	**16.25**
	P	0.01	0.8	0.002	0.01	0.04	0.03		0.01	0.1				0.4	0.6	0.4	0.2
Southampton 3	<20y	**3383**	**503**	**49.47**			**35.20**		**33.26**	**11.31**			**4.72**	**27.87**	**71.20**	**105.85**	**14.95**
	20-30y	**3469**	**517**	**49.64**			**35.16**		**33.58**	**11.51**			**4.81**	**28.25**	**70.88**	**104.82**	**14.94**
	>30y	**3505**	**526**	**50.01**			**35.29**		**33.51**	**11.45**			**4.80**	**27.88**	**70.69**	**105.59**	**15.05**
	P	0.5	0.6	0.2			0.7		0.7	0.6			0.9	0.4	0.6	0.2	0.9
Southampton 4	<20y	**3407**	**555**	**50.00**	**34.46**	**15.54**	**35.17**		**33.70**	**10.97**				**27.03**	**70.33**	**104.71**	**16.12**
	20-30y	**3559**	**521**	**50.33**	**33.81**	**16.52**	**35.18**		**34.33**	**11.45**				**27.69**	**69.93**	**102.65**	**14.78**
	>30y	**3622**	**541**	**52.00**	**34.40**	**16.60**	**35.39**		**34.60**	**11.64**				**27.27**	**69.38**	**102.46**	**14.94**
	P	0.5	0.6	0.2	0.098	0.3	0.7		0.4	0.2				0.6	0.5	0.5	0.5
Preston	<20y	**3268**	**505**	**51.62**			**35.21**							**23.93**	**68.35**		**15.62**
	20-30y	**3164**	**486**	**51.54**			**34.65**							**23.15**	**67.33**		**15.44**
	>30y	**3215**	**483**	**52.00**			**34.75**							**22.93**	**66.95**		**15.08**
	P	0.08	0.3	0.08			0.03							0.07	0.03		0.3
Sheffield	<20y	**3226**	**500**	**51.18**			**34.73**		**33.06**					**24.35**	**68.09**	**104.75**	**15.59**
	20-30y	**3265**	**497**	**51.09**			**34.59**		**32.88**					**24.57**	**67.84**	**104.88**	**15.34**
	>30y	**3366**	**514**	**51.44**			**34.81**		**33.15**					**24.75**	**67.79**	**104.68**	**15.40**
	P	<0.001	<0.001	<0.001			<0.001		0.004					0.3	0.6	0.6	0.5

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Farnborough	<20y	**3194**	**487**				**34.32**							**25.48**	**68.67**		**15.25**
	20-30y	**3312**	**505**				**34.60**							**25.69**	**68.41**		**15.29**
	>30y	**3375**	**513**				**34.73**							**25.83**	**68.41**		**15.27**
	P	0.002	0.1	0.09			0.05							0.7	0.9		0.99
Isle of Man	<20y	**3341**	**487**				**34.61**		**32.54**					**26.22**	**69.05**	**106.61**	**14.68**
	20-30y	**3365**	**495**				**34.64**		**32.49**					**26.80**	**69.31**	**106.74**	**14.72**
	>30y	**3422**	**489**				**34.78**		**32.52**					**26.96**	**69.36**	**107.15**	**14.29**
	P	0.6	0.8	0.7			0.6		0.97					0.2	0.7	0.8	0.4
Aberdeen	<20y	**3285**	**548**														**16.78**
	20-30y	**3222**	**531**														**16.62**
	>30y	**3160**	**459**														**13.99**
	P	0.7	0.04														0.02
Helsinki	<20y	**3312**	**494**				**34.53**							**26.69**	**69.33**		**14.99**
	20-30y	**3412**	**512**				**34.71**							**26.98**	**69.27**		**15.07**
	>30y	**3515**	**527**				**34.84**							**27.37**	**69.18**		**15.02**
	P	<0.001	<0.001	<0.001			<0.001							<0.001	0.4		0.7
Mysore 1	<20y	**2811**					**33.94**							**25.58**	**70.87**		
	20-30y	**2881**					**34.17**							**25.60**	**70.70**		
	>30y	**2999**					**34.23**							**26.13**	**70.48**		
	P	0.004		0.19			0.2							0.7	0.8		
Mysore 2	<20y	**2843**	**407**		**31.85**	**17.19**	**33.70**		**31.89**	**10.29**	**22.54**	**4.03**	**4.33**	**24.22**	**68.87**	**105.35**	**14.37**
	20-30y	**2965**	**418**		**32.24**	**16.91**	**34.08**		**32.24**	**10.44**	**22.72**	**4.28**	**4.55**	**24.95**	**69.39**	**112.66**	**14.15**
	>30y	**3088**	**448**		**32.76**	**16.66**	**34.52**		**32.69**	**10.74**	**23.16**	**4.67**	**4.87**	**25.56**	**69.90**	**115.73**	**14.61**
	P	0.001	0.02	0.4	0.005	0.07	<0.001		0.01	0.01	0.1	<0.001	0.002	0.007	0.08	0.5	0.3

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Pune 1	<20y	**2657**	**351**				**33.26**	**31.21**	**29.60**	**9.73**	**21.09**	**4.13**	**4.08**	**24.05**	**69.44**	**112.66**	**13.30**
	20-30y	**2758**	**369**				**33.38**	**31.53**	**29.91**	**9.84**	**21.21**	**4.33**	**4.29**	**24.61**	**69.28**	**111.88**	**13.39**
	>30y	**2989**	**402**				**33.50**	**32.46**	**30.91**	**10.28**	**21.83**	**4.91**	**4.65**	**25.30**	**68.03**	**108.56**	**13.78**
	P	<0.001	0.006	0.02			0.4	0.003	0.01	0.04	0.3	<0.001	0.003	0.006	0.1	0.03	0.7
Pune 2	<20y	**2777**	**384**				**33.41**	**31.02**	**28.97**	**9.42**	**20.28**	**4.15**	**3.96**	**26.12**	**70.42**	**115.73**	**13.80**
	20-30y	**2837**	**419**				**33.33**	**31.84**	**29.93**	**9.85**	**21.22**	**4.31**	**4.16**	**26.16**	**69.88**	**111.85**	**14.86**
	>30y	**2855**	**414**				**33.37**	**31.71**	**29.51**	**9.83**	**21.14**	**4.32**	**4.16**	**25.87**	**69.59**	**113.51**	**14.63**
	P	0.8	0.7	0.7			0.97	0.4	0.3	0.3	0.3	0.8	0.7	0.9	0.8	0.2	0.3
Kandy,Sri Lanka	<20y	**2557**					**33.10**							**22.91**	**70.98**		
	20-30y	**2737**					**33.40**							**23.16**	**69.23**		
	>30y	**2860**					**34.10**							**23.94**	**68.91**		
	P	0.003		0.002			0.02							0.04	0.06		
Beijing	<20y	**3012**	**415**		**33.07**	**15.84**	**31.56**							**25.67**	**64.58**		**13.74**
	20-30y	**3134**	**429**		**33.59**	**15.82**	**31.98**							**25.91**	**64.76**		**13.71**
	>30y	**3217**	**438**		**33.74**	**15.98**	**32.18**							**26.08**	**64.76**		**13.63**
	P	<0.001	0.006	<0.001	0.002	0.04	<0.001							0.1	0.9		0.7
Kasaji,Congo	<20y	**2670**	**362**				**33.68**	**28.93**		**9.29**	**20.42**	**3.54**	**3.54**	**25.29**	**70.96**		**13.77**
	20-30y	**2868**	**388**				**34.18**	**29.83**		**9.64**	**21.12**	**3.77**	**3.78**	**25.92**	**71.09**		**13.60**
	>30y	**2999**	**391**				**34.36**	**30.35**		**9.80**	**21.26**	**4.17**	**4.25**	**26.23**	**70.98**		**13.06**
	P	<0.001	0.02	<0.001			<0.001	0.001		<0.001	0.001	<0.001	<0.001	0.03	0.9		0.2
Imesi,Nigeria	<20y	**2749**	**448**				**33.53**	**32.51**						**26.30**	**71.18**		**16.63**
	20-30y	**2916**	**471**				**34.03**	**33.21**						**26.78**	**71.23**		**16.14**
	>30y	**3004**	**484**				**34.32**	**33.29**						**26.80**	**71.43**		**16.72**
	P	0.003	0.3	0.08			0.02	0.05						0.5	0.9		0.6

		Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
		g	g	cm	cm	cm	cm	cm	cm	cm	cm^2	mm	mm	kg/m^3	%	%	%
Kingston 1	<20y	**2997**	**456**	**48.23**	**32.46**	**15.77**	**34.23**	**32.12**	**31.98**	**10.05**				**26.93**	**71.11**	**107.19**	**15.21**
	20-30y	**3204**	**472**	**49.90**	**33.19**	**16.69**	**34.51**	**32.69**	**32.70**	**10.45**				**25.88**	**69.28**	**105.74**	**14.74**
	>30y	**3338**	**491**	**50.37**	**33.61**	**16.75**	**34.83**	**33.09**	**33.00**	**10.63**				**26.20**	**69.24**	**105.31**	**14.67**
	P	<0.001	0.1	<0.001	0.008	0.004	0.03	0.01	0.006	0.007				0.2	0.01	0.1	0.5
Kingston 2	<20y	**2853**	**434**	**49.06**	**33.01**	**16.01**	**34.03**							**24.18**	**67.19**		**15.32**
	20-30y	**3120**	**475**	**50.14**	**33.00**	**17.15**	**34.54**							**25.21**	**70.63**		**15.41**
	>30y	**3290**	**477**	**49.37**	**32.58**	**16.84**	**34.33**							**27.41**	**72.51**		**14.64**
	P	0.07	0.4	0.7	0.9	0.5	0.8							0.2	0.2		0.6

Appendix 2i Maternal age differences in lengths of rays for star graphs

	(20-30 years) – (<20 years)			(> 30 years) – (20-30 years)		
	Birthweight	CH length	Head	Birthweight	CH length	Head
Southampton 1	0.04	0.05	-0.01	0.001	0.06	0.01
Southampton 2	0.14	0.10	0.06	0.09	0.10	0.06
Southampton 3	0.08	0.03	-0.01	0.03	0.07	0.03
Southampton 4	0.14	0.07	0.002	0.05	0.13	0.05
Preston	-0.10	-0.02	-0.14	0.04	0.09	0.02
Sheffield	0.04	-0.02	-0.04	0.09	0.07	0.05
Farnborough	0.11	0.11	0.07	0.05	0.04	0.03
Isle of Man	0.02	-0.03	0.01	0.05	0.03	0.04
Helsinki	0.09	0.06	0.05	0.09	0.05	0.03
Mysore 1	0.06	0.08	0.06	0.10	0.03	0.02
Mysore 2	0.11	0.04	0.10	0.11	0.05	0.11
Pune 1	0.09	0.06	0.03	0.20	0.18	0.03
Pune 2	0.06	0.06	-0.02	0.02	0.05	0.01
Kandy, Sri Lanka	0.17	0.22	0.08	0.11	0.15	0.17
Beijing	0.11	0.10	0.11	0.07	0.06	0.05
Kasaji, Congo	0.18	0.17	0.12	0.11	0.09	0.04
Imesi, Nigeria	0.15	0.13	0.13	0.08	0.05	0.07
Kingston 1	0.19	0.33	0.07	0.12	0.09	0.08
Kingston 2	0.25	0.22	0.13	0.15	-0.14	-0.05

Appendix 3 Characterisation of maternal phenotypes

Appendix 3a Median maternal measurements

		Height (cm)	BMI (kg/m^2)	Head (cm)	AMA (cm^3)	Triceps (mm)	Birthweight (g)
Southampton1	Median	**163.0**	**26.5**	**54.8**			**3288**
	IQR	159.0,167.0	24.2,29.5	53.9,55.8			2948,3657
	N	554	553	557			506
Southampton2	Median	**163.0**	**26.8**	**55.3**	**32.1**	**19.6**	**3260**
	IQR	160.0,167.5	24.5,30.2	54.3,56.3	27.9,37.2	15.6,24.9	2910,3629
	N	520	514	521	513	514	476
Southampton3	Median	**163.0**	**26.8**				
	IQR	158.0,168.0	24.4,30.1				
	N	375	335				
Southampton4	Median	**165.1**	**24.5**				**3303**
	IQR	160.0,168.0	22.1,27.5				2927,3629
	N	101	95				84
Farnborough	Median	**162.6**	**24.7**				
	IQR	158.8,167.6	23.0,26.6				
	N	1646	1594				
Isle of Man	Median	**163.0**	**22.8**				**3289**
	IQR	159.3,167.4	21.0,25.2				2948,3629
	N	388	386				304
Aberdeen	Median	**157.5**	**24.8**				
	IQR	153.7,161.3	23.0,26.5				
	N	233	215				
Helsinki	Median	**158.0**					
	IQR	154.0,162.0					
	N	5620					
Mysore 1	Median	**152.4**	**21.4**				**2720**
	IQR	147.7,155.7	19.7,23.3				2440,3008
	N	890	45				412
Mysore 2	Median	**154.5**	**23.3**	**53.5**	**21.4**	**16.8**	**2807**
	IQR	151.0,158.0	21.0,25.9	52.4,54.5	18.5,24.4	12.3,24.4	2523,3033
	N	597	597	568	596	596	63
Pune 1	Median	**152.0**	**20.3**	**52.2**	**24.2**	**9.0**	
	IQR	148.5,155.5	19.2,21.5	51.3,53.2	21.0,26.7	7.1,11.3	
	N	633	610	609	610	610	
Pune 2	Median	**152.8**		**53.6**			
	IQR	149.2,156.7		51.9,55.0			
	N	258		258			
Kandy,	Median	**150.7**	**20.0**				
Sri Lanka	IQR	146.7,154.7	18.7,22.2				
	N	446	434				
Beijing	Median	**155.0**	**23.6**				
	IQR	152.0,158.8	22.0,25.2				
	N	2118	1252				
Kasaji,	Median	**154.3**	**21.7**		**24.8**	**11.0**	
Congo	IQR	151.0,158.8	20.3,23.4		21.9,28.5	8.8,13.6	
	N	338	335		183	183	
Imesi,	Median	**160.0**	**21.6**				
Nigeria	IQR	154.9,162.6	20.4,22.7				
	N	263	210				
Kingston 1	Median	**163.5**	**26.9**			**17.4**	
	IQR	158.8,167.1	24.0,30.2			13.0,22.8	
	N	489	429			429	
Kingston 2	Median	**163.0**	**24.1**		**34.6**	**10.2**	
	IQR	157.0,165.0	22.6,27.0		31.1,42.0	8.6,14.2	
	N	66	54		55	55	

		Height (cm)
WHO Sweden	Median	**168.0**
	IQR	164.0,171.0
	N	505
WHO Australia	Median	**164.0**
	IQR	160.0,168.0
	N	622
WHO Chile	Median	**155.0**
	IQR	151.0,158.0
	N	688
WHO Guatemala	Median	**153.0**
	IQR	149.0,156.0
	N	294
WHO India	Median	**154.0**
	IQR	151.0,158.0
	N	504
WHO China	Median	**155.0**
	IQR	152.0,157.0
	N	541
WHO Nigeria	Median	**159.0**
	IQR	156.0,164.0
	N	512

Appendix 4 Mother to baby relationships

Appendix 4a Age and parity effects on maternal anthropometry

p≥0.1 p<0.1 p<0.05 p<0.01

Height (cm)	Individual				Simultaneous	
	Age (yrs) Linear	Quadratic	Parity Linear	Quadratic	Age (yrs) Linear	Parity Linear
Southampton 1	0.11		-0.74		0.17	-1.06
Southampton 2	0.08		-0.61		0.13	-0.81
Southampton 3	0.19		0.04		0.22	-0.42
Southampton 4	0.10	-0.07	-0.72		0.18	-1.09
Farnborough	0.12		-0.16		0.16	-0.49
Isle of Man	0.10					
Aberdeen	0.17	-0.03				
Helsinki	-0.05		-0.13		-0.06	0.02
Mysore 1	0.05		0.20		0.03	0.16
Mysore 2	-0.04		-0.90		0.02	-0.94
Pune 1	-0.06		-0.49		0.06	-0.62
Pune 2	-0.05		-1.53		-0.02	-1.51
Kandy, Sri Lanka	0.13		0.13		0.15	-0.17
Beijing	-0.02	-0.01	-0.34		0.04	-0.44
Kasaji, Congo	0.16	-0.01	0.60		0.13	0.14
Imesi, Nigeria	0.16		0.62		0.16	0.05
Kingston 1	-0.07		-0.23		-0.06	-0.08
Kingston 2	0.08		-0.08		0.25	-0.80
WHO Sweden	0.01					
WHO Australia	0.01					
WHO Chile	-0.07					
Who Guatemala	-0.04					
WHO India	0.03					
WHO China	-0.05					
WHO Nigeria	-0.06					

BMI (kg/m^2) logged	Individual				Simultaneous	
	Age (yrs) Linear	Quadratic	Parity Linear	Quadratic	Age (yrs) Linear	Parity Linear
Southampton 1	0.002		0.01		0.002	0.003
Southampton 2	0.004		0.02		0.003	0.01
Southampton 3	0.001		0.01		-0.0003	0.01
Southampton 4	0.01		0.03		0.01	0.02
Farnborough	0.002		0.01		0.001	0.01
Isle of Man	0.003					
Aberdeen	0.002					
Mysore 1	0.01		0.03		0.01	-0.0003
Mysore 2	0.01		0.03		0.01	0.01
Pune 1	0.001	0.0004	0.0004		0.002	-0.003
Kandy, Sri Lanka	0.002		-0.005		0.003	-0.01
Beijing	0.002	0.0002	0.01		0.001	0.01
Kasaji, Congo	0.004	-0.0004	0.02		0.002	0.01
Imesi, Nigeria	0.001		0.005		-0.0001	0.01
Kingston 1	0.01		0.04	-0.02	0.01	0.01
Kingston 2	0.01		0.02	-0.02	0.004	0.01

Head (cm)	Individual				Simultaneous	
	Age (yrs)		Parity		Age (yrs)	Parity
	Linear	Quadratic	Linear	Quadratic	Linear	Linear
Southampton 1	0.02		-0.01		0.02	-0.05
Southampton 2	0.01		-0.03		0.01	-0.05
Mysore 2	0.03		0.05		0.03	-0.0004
Pune 1	0.01		0.04		0.01	0.01

AMA (cm^2) logged	Individual				Simultaneous	
	Age (yrs)		Parity		Age (yrs)	Parity
	Linear	Quadratic	Linear	Quadratic	Linear	Linear
Southampton 2	0.003	-0.001	0.02		0.002	0.02
Mysore 2	0.01		0.05		0.01	0.04
Pune 1	0.005		0.02		0.002	0.01
Kasaji, Congo	0.01	-0.001	0.04		0.01	0.01
Kingston 2	0.01		0.05		0.01	0.02

Triceps (mm)	Individual				Simultaneous	
	Age (yrs)		Parity		Age (yrs)	Parity
	Linear	Quadratic	Linear	Quadratic	Linear	Linear
Southampton 2	0.01	-0.002	0.01		0.01	0.0001
Mysore 2	0.02		0.04		0.02	0.002
Pune 1	-0.01	0.001	-0.05	0.03	-0.0001	-0.05
Kasaji, Congo	0.01		0.03		-0.003	0.04
Kingston 1	0.03		0.06	-0.06	0.03	0.002
Kingston 2	0.01		0.03	-0.09	0.01	0.001

Appendix 4b Maternal age, parity, neonatal sex and gestation effects on neonatal anthropometry

P≥0.1 p<0.1 p<0.05 p<0.01

Birthweight (g)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	3.68		48.97		-182.67	21.28		2.39	54.41	-184.39	21.56
Southampton 2	4.33		43.37		-104.49	21.24	-0.37	8.17	34.65	-131.62	22.15
Southampton 3	2.51		19.37		-125.72	21.00		3.36	41.00	-152.96	22.72
Southampton 4	0.66		47.38		-68.48	26.95		-0.20	50.74	-76.75	27.40
Farnborough	9.41	-0.84	49.18		-128.59	16.83	-0.42	9.39	33.70	-143.84	17.88
Isle of Man	1.92				-99.33	12.62		5.10		-130.25	13.63
Aberdeen	-6.91				-76.80	12.18		-8.00		-96.77	12.81
Mysore 1	16.43		40.78	-19.47	-143.38	7.62	-0.36	14.33	8.60	-144.65	7.74
Mysore 2	9.83		33.81		-90.55	12.13	-0.71	10.38	23.74	-106.77	13.37
Pune 1	12.63		53.12		-113.73	15.84		6.25	49.63	-119.89	16.63
Kandy, Sri Lanka	12.19		48.45		-20.49	17.17		7.30	32.18	-7.16	14.72
Beijing	7.75		54.62		-130.81	11.86	-0.32	2.95	46.82	-140.62	12.23
Kasaji, Congo	23.35	-1.16	107.92	-26.49	-24.74	18.18	-0.41	2.53	84.24	-10.93	15.32
Imesi, Nigeria	3.73		42.98		-96.68			-6.52	70.67	-98.44	
Kingston 1	13.27		30.88	-37.07	-169.51	13.93		13.26	9.23	-173.06	15.54
Kingston 2	24.00		31.90	-127.32	-380.94	14.74	-2.10	38.31	-38.29	-325.75	16.92

Placental weight (g)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	1.37		11.45	-11.21	-21.06	1.59		0.94	10.49	-21.29	1.64
Southampton 2	-0.52		17.82		-16.22	1.65		-1.25	20.30	-17.71	1.66
Southampton 3	0.47		0.93		-26.87	3.50		1.10	3.80	-31.89	3.80
Southampton 4	-2.05		-8.30		-15.20	4.21		-0.92	-7.18	-23.73	4.19
Farnborough	0.58		12.06		-15.42	1.45	-0.08	-0.15	12.66	-16.68	1.53
Isle of Man	-0.34				-10.37	1.64		0.06		-13.77	1.82
Aberdeen	0.68				24.72	1.48		0.44		22.29	1.37
Mysore 2	1.58		9.25	-8.27	2.05	1.11	-0.10	1.27	7.68	0.60	1.22
Pune 1	2.22		6.66		-10.42	1.31		1.84	3.65	-10.88	1.41
Beijing	1.22		6.66		-13.14	1.19		0.71	4.98	-14.45	1.25
Kasaji, Congo	2.31		7.59		11.38	1.62		2.23	-1.48	10.83	1.32
Imesi, Nigeria	-0.34		5.69		-27.95			-2.60	15.17	-24.25	
Kingston 1	1.28		3.44		-16.92	1.63		1.24	1.83	-17.52	1.81
Kingston 2	0.17		2.67		-31.39	2.25	-0.19	-1.29	11.2	-32.04	2.36

CH length (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	0.03		0.07		-1.12	0.09		0.04	0.03	-1.14	0.09
Southampton 2	0.03		0.15		-1.00	0.10	-0.002	0.06	0.08	-1.15	0.10
Southampton 3	0.02		0.02		-0.67	0.09		0.03	0.08	-0.79	0.09
Southampton 4	0.01		0.21		-0.82	0.12		0.01	0.16	-0.89	0.12
Farnborough	0.04		0.18		-0.67	0.06		0.04	0.12	-0.72	0.06
Isle of Man	0.002				-0.73	0.06		0.02		-0.87	0.06
Mysore 1	0.05		0.08		-0.66	0.02		0.05	-0.03	-0.66	0.02
Mysore 2	0.01		0.02		-0.54	0.06	-0.003	0.02	0.02	-0.63	0.07
Pune 1	0.04		0.12		-0.72	0.09		0.03	0.10	-0.75	0.09
Kandy, Sri Lanka	0.11		0.37		-0.89	0.11		0.07	0.17	-0.77	0.08
Beijing	0.03		0.16		-0.77	0.06	-0.002	0.02	0.11	-0.83	0.06
Kasaji, Congo	0.11	-0.01	0.48		-0.59	0.06		0.02	0.31	-0.52	0.09
Imesi, Nigeria	0.02	-0.01	0.14		-0.70	0.10		0.002	0.15	-0.73	
Kingston 1	0.05		0.11		-1.07	0.07		0.05	0.04	-1.11	0.08
Kingston 2	0.07		0.04		-1.66	0.05		0.16	-0.27	-1.53	0.05

CR length (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	0.01		0.02		-0.77	0.06		0.01	0.02	-0.77	0.06
Southampton 2	0.02		0.13		-0.61	0.09		0.04	0.08	-0.71	0.07
Southampton 4	0.005		0.15		-0.26	0.03		0.002	0.16	-0.30	0.09
Mysore 2	0.03		0.04		-0.38	0.05	-0.003	0.04	-0.004	-0.45	0.05
Beijing	0.02		0.09		-0.47	0.03	-0.001	0.02	0.05	-0.50	0.04
Kingston 1	0.04		0.01		-0.59	0.04		0.05	-0.08	-0.61	0.04
Kingston 2	0.02		-0.13		-1.53	0.03		0.12	-0.37	-1.35	0.03

Leg length (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	0.02		0.05		-0.36	0.03		0.03	0.01	-0.37	0.03
Southampton 2	0.01		0.03		-0.38	0.03		0.02	0.002	-0.43	0.03
Southampton 4	0.01		0.05		-0.57	0.03		0.01	-0.001	-0.59	0.03
Mysore 2	-0.02		-0.03		-0.13	0.02		-0.02	0.03	-0.16	0.02
Beijing	0.01		0.08	0.05	-0.30	0.02	-0.001	0.01	0.06	-0.32	0.02
Kingston 1	0.01		0.10		-0.48	0.03		0.003	0.12	-0.51	0.04
Kingston 2	0.05		0.17		-0.13	0.02		0.04	0.11	-0.19	0.02

Head (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	0.01		0.08		-0.75	0.05		0.01	0.08	-0.76	0.06
Southampton 2	0.02		0.13		-0.71	0.05		0.03	0.09	-0.79	0.05
Southampton 3	-0.001		0.03		-0.58	0.06		0.004	0.10	-0.66	0.06
Southampton 4	0.01		0.13		-0.70	0.06		0.004	0.08	-0.73	0.06
Farnborough	0.02		0.07		-0.53	0.03		0.02	0.03	-0.56	0.03
Isle of Man	-0.01				-0.52	0.03		0.01		-0.60	0.04
Mysore 1	0.03		-0.02		-0.52	0.02	-0.001	0.05	-0.13	-0.52	0.03
Mysore 2	0.02		0.03		-0.57	0.04	-0.002	0.03	0.001	-0.62	0.04
Pune 1	0.01		0.04		-0.61	0.06		0.02	0.04	-0.62	0.06
Kandy, Sri Lanka	0.06		0.22		-0.70	0.05		0.05	0.10	-0.64	0.03
Beijing	0.02	-0.003	0.17	-0.06	-0.47	0.03	-0.001	0.003	0.16	-0.49	0.03
Kasaji, Congo	0.05	-0.004	0.22		-0.42	0.06		0.01	0.13	-0.39	0.06
Imesi, Nigeria	0.02		0.16		-0.61			-0.02	0.24	-0.63	
Kingston 1	0.04		0.07		-0.74	0.04		0.04	0.01	-0.76	0.05
Kingston 2	0.02		0.003		-1.04	0.04	-0.01	0.06	-0.07	-0.96	0.04

Chest (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Pune 1	0.04		0.18		-0.38	0.07		0.01	0.19	-0.41	0.07
Kasaji, Congo	0.08	-0.01	0.44	-0.16	0.04	0.07		-0.03	0.49	0.14	0.06
Imesi, Nigeria	0.02		0.18		-0.50			-0.02	0.26	-0.52	
Kingston 1	0.03		0.06		-0.55	0.07		0.04	0.04	-0.59	0.07

Abdomen (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	0.02		0.21		-0.39	0.08		0.01	0.22	-0.39	0.08
Southampton 2	0.01		0.24		-0.19	0.08	-0.002	0.01	0.23	-0.27	0.08
Southampton 3	-0.01		0.09		-0.33	0.08		-0.01	0.22	-0.41	0.08
Southampton 4	0.001		0.25		-0.21	0.10		-0.01	0.29	-0.22	0.10
Isle of Man	-0.02				-0.33	0.05		-0.003		-0.44	0.06
Mysore 2	0.04		0.11		-0.11	0.06	-0.003	0.04	0.07	-0.19	0.06
Pune 1	0.05		0.23		-0.05	0.06		0.02	0.23	-0.07	0.06
Kingston 1	0.03		0.07		-0.52	0.06		0.03	0.06	-0.55	0.07

MUAC (cm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	0.01		0.12		-0.19	0.03		0.004	0.12	-0.19	0.03
Southampton 2	0.002		0.07		-0.04	0.03		0.01	0.06	-0.07	0.03
Southampton 3	-0.01		0.07		-0.09	0.04		-0.01	0.15	-0.12	0.04
Southampton 4	0.02		0.17		-0.04	0.04		0.02	0.14	-0.005	0.04
Mysore 2	0.02		0.03		-0.10	0.02	-0.001	0.03	-0.004	-0.13	0.02
Pune 1	0.01		0.07		-0.06	0.03		0.002	0.09	-0.07	0.03
Kasaji, Congo	0.04	-0.002	0.19	-0.06	0.12	0.03	-0.001	-0.01	0.21	0.15	0.02
Kingston 1	0.02		0.04		-0.20	0.02		0.02	0.01	-0.20	0.02

AMA (cm^2)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Mysore 2	0.04		0.004		-0.35	0.04	-0.002	0.05	-0.06	0.41	0.05
Pune 1	0.003		0.08		-0.19	0.06		-0.01	0.13	-0.21	0.07
Kasaji, Congo	0.06	-0.01	0.35	-0.13	0.10	0.06		-0.03	0.42	0.15	0.05

Triceps (mm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Mysore 2	0.03		0.10		0.12	0.01	-0.001	0.03	0.06	0.11	0.01
Pune 1	0.04		0.14		0.05	0.02		0.02	0.11	0.04	0.02
Kasaji, Congo	0.04		0.18		0.28	0.02		0.01	0.12	0.30	0.01

Subscapular (mm)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 3	-0.0002		0.04		0.18	0.02		-0.005	0.09	0.16	0.02
Mysore 2	0.03		0.13		0.14	0.01	-0.001	0.02	0.10	0.12	0.02
Pune 1	0.03		0.16	-0.06	0.13	0.01	-0.001	-0.002	0.17	0.13	0.01
Kasaji, Congo	0.05		0.19		0.38	0.02		0.02	0.11	0.40	0.01

PI (kg/m^3)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	-0.01		0.28		0.42	0.03		-0.03	0.36	0.44	0.03
Southampton 2	-0.004		0.16		0.79	0.02		-0.02	0.19	0.78	0.02
Southampton 3	-0.01		0.13		0.15	0.02		-0.03	0.23	0.14	0.03
Southampton 4	-0.01		0.10		0.75	0.03		-0.02	0.22	0.79	0.03
Farnborough	0.01		0.13		-0.01	0.03		0.003	0.13	-0.03	0.03
Isle of Man	0.02				0.36	0.01		0.02		0.33	0.01
Mysore 1	0.07		0.27	-0.22	-0.22	0.04		0.04	0.16	-0.26	0.04
Mysore 2	0.06		0.21		0.06	0.01		0.05	0.12	0.04	0.01
Pune 1	0.07		0.35		-0.03	0.004		0.01	0.32	-0.04	0.01
Kandy, Sri Lanka	0.08		0.27		0.85	0.07		0.05	0.19	0.95	0.06
Beijing	0.02		0.18	-0.12	0.16	0.01		-0.01	0.21	0.16	0.01
Kasaji, Congo	0.04		0.22		0.78	0.002		-0.02	0.32	0.82	-0.004
Imesi, Nigeria	0.01		0.18		0.003			-0.06	0.41	0.05	
Kingston 1	0.02		0.10		0.27	0.004		0.01	0.09	0.29	0.01
Kingston 2	0.10		0.45		-1.24	0.04		0.0004	0.61	-1.53	0.06

Head/length (%)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	-0.02		0.06		0.06	-0.01		-0.04	0.13	0.08	-0.01
Southampton 2	-0.005		0.04		-0.02	-0.04		-0.02	0.07	0.03	-0.04
Southampton 3	-0.01		0.01		-0.22	-0.01		-0.02	0.05	-0.20	-0.01
Southampton 4	-0.01		-0.01		-0.24	-0.04		-0.01	-0.02	-0.21	-0.04
Farnborough	-0.01		-0.09		-0.16	-0.03		-0.01	-0.08	-0.14	-0.03
Isle of Man	-0.01				-0.02	-0.01		-0.01		0.01	-0.01
Mysore 1	-0.01		-0.13		-0.17	0.03		0.02	-0.20	-0.17	0.03
Mysore 2	0.03		0.02		-0.38	-0.02		0.03	-0.04	-0.36	-0.01
Pune 1	-0.03		-0.09		-0.25	0.002		-0.02	-0.04	-0.25	0.001
Kandy, Sri Lanka	-0.07		-0.21		0.03	-0.11		-0.04	-0.11	-0.13	-0.10
Beijing	0.01	-0.004	0.13	-0.15	0.07	-0.02		-0.03	0.19	0.10	-0.02
Kasaji, Congo	-0.06		-0.26		0.02	-0.02		-0.01	-0.22	-0.01	-0.02
Imesi, Nigeria	0.01		0.21		-0.18			-0.05	0.41	-0.17	
Kingston 1	-0.004		-0.02		0.04	-0.01		-0.004	-0.02	0.05	-0.01
Kingston 2	-0.05		-0.06		0.09	0.01		-0.10	0.24	0.06	0.003

Head/abdomen (%)	Individual							Simultaneous			
	Age (years)		Parity		Sex	Gestation (days)		Age (years)	Parity	Sex	Gestation (days)
	Linear	Quadratic	Linear	Quadratic	Linear	Linear	Quadratic	Linear	Linear	Linear	Linear
Southampton 1	-0.04		-0.43		-1.03	-0.08		-0.02	-0.44	-1.03	-0.08
Southampton 2	0.04	0.01	-0.35		-1.53	-0.09	0.004	0.06	-0.43	-1.50	-0.08
Southampton 3	0.02		-0.24		-0.73	-0.07		0.05	-0.45	-0.69	-0.07
Southampton 4	0.02		-0.39		-1.38	-0.14		0.04	-0.64	-1.45	-0.13
Isle of Man	0.04				-0.52	-0.07		0.03		-0.40	-0.07
Mysore 2	-0.05		-0.23		-1.38	-0.07	0.004	-0.05	-0.19	-1.30	-0.07
Pune 1	-0.16		-0.75		-1.87	0.0001	0.01	-0.02	-0.69	-1.85	-0.01
Kingston 1	-0.02		-0.13		-0.38	-0.06		-0.02	-0.17	-0.34	-0.07

Placenta /birthweight (%)	Individual Age (years) Linear	Quadratic	Parity Linear	Quadratic	Sex Linear	Gestation (days) Linear	Quadratic	Simultaneous Age (years) Linear	Parity Linear	Sex Linear	Gestation (days) Linear
Southampton 1	0.03		0.13		0.27	-0.05		0.02	0.07	0.25	-0.05
Southampton 2	-0.04		0.31		0.05	-0.06	0.003	-0.08	0.42	0.15	-0.06
Southampton 3	0.01		-0.08		-0.15	0.01		0.02	-0.11	-0.17	0.01
Southampton 4	-0.06		-0.38		0.02	0.003		-0.04	-0.33	-0.16	-0.001
Farnborough	-0.02		0.14		0.12	-0.03		-0.05	0.23	0.15	-0.03
Isle of Man	-0.02				0.20	-0.01		-0.02		0.23	-0.01
Aberdeen	0.02				1.19	-0.02		0.02		1.23	-0.02
Mysore 2	0.01		0.14		0.46	-0.02		-0.01	0.13	0.50	-0.03
Pune 1	0.02		-0.001		0.17	-0.03		0.04	-0.09	0.17	-0.03
Beijing	0.002		-0.04		0.16	-0.01	0.001	0.01	-0.06	0.17	-0.01
Kasaji, Congo	-0.04		-0.30	0.15	0.44	-0.03		0.06	-0.48	0.40	-0.02
Imesi, Nigeria	-0.02		0.02		-0.42			-0.05	0.20	-0.34	
Kingston 1	-0.02		-0.05		0.26	-0.01		-0.02	-0.02	0.26	-0.02
Kingston 2	-0.11		-0.11		0.85	0.002		-0.19	0.39	0.65	-0.01

Appendix 4c Relationships between maternal and neonatal anthropometry (adjusted for neonatal sex and gestation)

P≥0.1 p<0.1 p<0.05 p<0.01

Maternal predictors	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
Birthweight (g)	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Southampton 1	15.22	0.69	17.86		52.54						204.58	
Southampton 2	10.64		16.15	-3.05	45.47		3.54		11.07		167.99	
Southampton 3	16.65		25.59									
Southampton 4	14.74		29.50								255.67	
Farnborough	14.52		32.59	-2.51								
Isle of Man	18.45		13.85								152.30	
Aberdeen	16.13		37.83									
Helsinki	16.20	0.24										
Mysore 1	10.20		48.94								238.19	
Mysore 2	6.73	-1.23	41.46		52.45		9.85		12.20		412.68	
Pune 1	9.98		39.49		31.61		4.07		6.21			
Pune 2	20.06											
Kandy, Sri Lanka	17.46		34.55									
Beijing	13.50		33.99	-2.52								
Kasaji, Congo	20.73		55.71				25.18		22.34			
Imesi, Nigeria	17.41		53.67									
Kingston 1	7.76		23.44						12.35			
Kingston 2	24.50		32.25				13.46		26.44			
WHO Sweden	5.12											
WHO Australia	15.17											
WHO Chile	8.57											
WHO Guatemala	9.97											
WHO India	11.76											
WHO China	8.18											
WHO Nigeria	5.51											

Maternal predictors Placental weight (g)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	3.31	0.15	3.62		12.33						40.93	
Southampton 2	1.08		2.76	-0.61	3.00		0.68		1.91		22.21	
Southampton 3	1.72		5.55									
Southampton 4	3.25		5.55								23.29	
Farnborough	1.14		7.13									
Isle of Man	2.10		1.76								10.54	
Aberdeen	1.80		7.36									
Helsinki	1.96											
Mysore 2	1.02	-0.19	6.66		8.88		2.35		1.76	-0.09	22.52	
Pune 1	1.49		6.26		3.40		0.20		1.14			
Pune 2	2.22											
Beijing	1.91		5.68	-0.49								
Kasaji, Congo	2.24		7.50				3.38		1.22			
Imesi, Nigeria	2.97		14.15									
Kingston 1	1.19		5.44						2.62			
Kingston 2	1.22		5.83				2.23		6.05			

Maternal predictors	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
CH length (cm)	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Southampton 1	0.07	0.002	0.05		0.18						0.47	
Southampton 2	0.08		0.01	-0.01	0.17		-0.01		0.02		0.67	
Southampton 3	0.09		0.05									
Southampton 4	0.05		0.02								0.78	
Farnborough	0.07		0.12	-0.01								
Isle of Man	0.08		0.01								0.67	
Helsinki	0.05	0.001										
Mysore 1	0.04		0.42								0.51	
Mysore 2	0.05	-0.005	0.11		0.16		0.02		0.03		1.59	
Pune 1	0.08		0.09		0.24		0.01		0.01			
Pune 2	0.08											
Kandy, Sri Lanka	0.16		0.21									
Beijing	0.07		0.11	-0.01								
Kasaji, Congo	0.09		0.21				0.12		0.07			
Imesi, Nigeria	0.07		0.14									
Kingston 1	0.06		0.10						0.07			
Kingston 2	0.16		0.12				0.09		0.09			
WHO Sweden	0.03											
WHO Australia	0.08											
WHO Chile	0.06											
WHO Guatemala	0.08											
WHO India	0.07											
WHO China	0.02											
WHO Nigeria	0.04											

Maternal predictors CR length (kg)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	0.04	0.002	0.05		0.14						0.39	
Southampton 2	0.04		0.02	-0.01	0.13		-0.002		0.02		0.45	
Southampton 4	0.005		0.06								0.79	
Mysore 2	0.03	-0.005	0.11		0.14		0.04		0.02		1.51	
Beijing	0.04		0.07									
Kingston 1	0.04		0.09						0.06			
Kingston 2	0.10		0.01				0.04		-0.01			

Maternal predictors Leg length (kg)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	0.03		0.01		0.05						0.09	
Southampton 2	0.04		-0.01		0.03		-0.01		0.002		0.21	0.15
Southampton 4	0.05		-0.04								-0.01	
Mysore 2	0.02		-0.004		0.01		-0.02		0.01		0.08	
Beijing	0.03		0.04									
Kingston 1	0.02		0.003						0.004			
Kingston 2	0.06		0.12				0.05		0.10			

Maternal predictors Head (cm)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	0.03	0.002	0.05		0.20						0.43	
Southampton 2	0.02		0.05	-0.01	0.15		0.01		0.03		0.26	
Southampton 3	0.03		0.07									
Southampton 4	0.02		0.09								0.38	
Farnborough	0.03		0.08	-0.01								
Isle of Man	0.03		0.04								0.16	
Helsinki	0.03	0.001										
Mysore 1	0.02		-0.02								0.26	
Mysore 2	0.02	-0.002	0.10	-0.01	0.19		0.03		0.03		1.20	
Pune 1	0.01		0.11		0.16		0.01		0.02			
Pune 2	0.06											
Kandy, Sri Lanka	0.04		0.08									
Beijing	0.03		0.07									
Kasaji, Congo	0.03		0.14				0.06		0.03			
Imesi, Nigeria	0.02		0.14									
Kingston 1	0.01		0.06						0.04			
Kingston 2	0.08		-0.01				0.01		-0.001			
WHO Australia	0.01											
WHO Sweden	0.03											
WHO Chile	0.02											
WHO Guatemala	0.02											
WHO India	0.03											
WHO China	0.01											
WHO Nigeria	0.003											

Maternal predictors Chest (cm)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Pune 1	0.03		0.12		0.13		-0.005		0.01			
Pune 2	0.06											
Kasaji, Congo	0.07		0.21				0.10		0.07			
Imesi, Nigeria	0.06		0.09									
Kingston 1	0.04		0.09						0.05			
WHO Sweden	0.03											
WHO Australia	0.04											
WHO Chile	0.03											
WHO India	0.04											
WHO China	0.01											
WHO Nigeria	0.03											

Maternal predictors Abdomen (cm)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	0.05		0.06		0.11						0.63	
Southampton 2	0.03		0.06	-0.01	0.07		0.01		0.04		0.49	
Southampton 3	0.06		0.07									
Southampton 4	0.01		0.10								0.77	
Isle of Man	0.04		0.02								0.14	
Mysore 2	0.03	-0.004	0.14		0.18		0.04		0.04		1.49	
Pune 1	0.01		0.12		0.13		-0.002		0.01			
Pune 2	0.09											
Kingston 1	0.03		0.08	-0.01					0.04			

Maternal predictors MUAC (cm)	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Southampton 1	0.02		0.04	-0.004	0.07						0.39	
Southampton 2	0.01		0.04	-0.004	0.05		0.01		0.02		0.29	
Southampton 3	0.02		0.04									
Southampton 4	0.01		0.07								0.37	
Mysore 2	0.01	-0.002	0.07		0.09		0.02		0.02		1.08	
Pune 1	0.02		0.06		0.08		0.01		0.01			
Pune 2	0.04											
Kasaji, Congo	0.03		0.08				0.04		0.02			
Kingston 1	0.005		0.05						0.03			

Maternal predictors AMA (cm^2)	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Mysore 2	0.01		0.12		0.14		0.03		0.04		2.19	
Pune 1	0.05		0.10		0.15		0.01		0.01			
Pune 2	0.08											
Kasaji, Congo	0.06		0.19	-0.03			0.09		0.05			

Maternal predictors Triceps (mm)	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Mysore 2	0.01	-0.002	0.08		0.09		0.02		0.03		0.65	
Pune 1	-0.001		0.07		0.06		0.01		0.01			
Pune 2	0.02											
Kasaji, Congo	0.01		0.05				0.01		0.01			

Maternal predictors Subscapular (mm)	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Southampton 3	0.01		0.05									
Mysore 2	0.003	-0.003	0.07		0.03		0.02		0.02		0.50	
Pune 1	-0.0003		0.04		0.05		0.01		0.003			
Pune 2	0.02											
Kasaji, Congo	0.01		0.06				0.01		0.01			

Maternal predictors PI (kg/m^3)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	0.004		0.06		0.08				0.78		0.78	
Southampton 2	-0.05		0.11	-0.01	0.02		0.04		0.05		0.27	
Southampton 3	-0.01		0.11									
Southampton 4	0.04		0.19								0.85	
Farnborough	0.01		0.05									
Isle of Man	0.02		0.09	-0.01							0.20	
Helsinki	0.04											
Mysore 1	0.03		-0.32								1.50	
Mysore 2	-0.02		0.18		0.20		0.06		0.06		1.06	
Pune 1	-0.04		0.21		-0.05		0.02		0.03			
Pune 2	0.05											
Kandy, Sri Lanka	-0.03		0.17									
Beijing	0.003		0.10									
Kasaji, Congo	0.04		0.16				0.04		0.08			
Imesi, Nigeria	0.02		0.28									
Kingston 1	-0.02		0.02						-0.01			
Kingston 2	-0.03		-0.03				-0.04		-0.02			
WHO Australia	-0.01											
WHO Sweden	-0.02											
WHO Chile	-0.02											
WHO Guatemala	-0.04											
WHO India	-0.01											
WHO China	0.03											
WHO Nigeria	-0.02											

Maternal predictors Head/length (%)	Height (cm) Linear	Quadratic	BMI (kg/m^2) Linear	Quadratic	Head (cm) Linear	Quadratic	AMA (cm^2) Linear	Quadratic	Triceps (mm) Linear	Quadratic	Birthweight (kg) Linear	Quadratic
Southampton 1	-0.03		0.03		0.14						0.17	
Southampton 2	-0.07		0.08		0.06		0.04		0.02	-0.003	-0.39	
Southampton 3	-0.06		0.06									
Southampton 4	-0.03		0.14								-0.30	
Farnborough	-0.03		-0.01									
Isle of Man	-0.06		0.05								-0.60	
Helsinki	-0.01											
Mysore 1	-0.03		-0.60								-0.22	
Mysore 2	-0.04		0.04	-0.02	0.15		0.04		0.01		0.19	
Pune 1	-0.09		0.10		0.01		-0.01		0.02			
Pune 2	-0.01											
Kandy, Sri Lanka	-0.13		-0.10									
Beijing	-0.03		0.003									
Kasaji, Congo	-0.06		-0.01				-0.01		-0.05			
Imesi, Nigeria	-0.07		0.12									
Kingston 1	-0.05		-0.03						-0.02			
Kingston 2	-0.06		-0.16				-0.12		0.17			
WHO Australia	-0.03											
WHO Sweden	-0.06											
WHO Chile	-0.05											
WHO Guatemala	-0.06											
WHO India	-0.04											
WHO China	-0.02											
WHO Nigeria	-0.05											

Maternal predictors	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
Head/abdomen (%)	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Southampton 1	-0.07		-0.04		0.27						-0.79	
Southampton 2	-0.04		-0.04		0.25		0.01		-0.03		-0.74	
Southampton 3	-0.08		-0.03									
Southampton 4	0.02		-0.07								-1.22	
Isle of Man	-0.04		0.04								0.08	
Mysore 2	-0.03		-0.17	-0.03	0.15		-0.001		-0.07		-2.07	
Pune 1	-0.01		-0.10		0.03		0.02		0.02			
Pune 2	-0.16											
Kingston 1	-0.05		-0.09	0.02					-0.02			

Maternal predictors	Height (cm)		BMI (kg/m^2)		Head (cm)		AMA (cm^2)		Triceps (mm)		Birthweight (kg)	
Placenta/ birthweight (%)	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Southampton 1	0.03		0.02		0.12						0.25	
Southampton 2	-0.01		0.02		-0.10		0.01		0.003		-0.09	
Southampton 3	-0.02		0.05									
Southampton 4	0.03		0.05								-0.40	
Farnborough	-0.03		0.06									
Isle of Man	-0.02		-0.01								-0.33	
Aberdeen	-0.02		0.04									
Helsinki	-0.02											
Mysore 2	0.003		0.02		0.06		0.03		0.01		-1.32	
Pune 1	-0.01		0.03		-0.03		-0.01		0.0001			
Pune 2	-0.03											
Beijing	0.001		0.03									
Kasaji, Congo	-0.02		0.0001				-0.002		-0.07			
Imesi, Nigeria	-0.02		0.08									
Kingston 1	0.003		0.05						0.02			
Kingston 2	-0.06		0.01				0.004		0.07			

Appendix 4d Derivation of ellipses for maternal height and BMI

The following Matlab program was used to calculate co-ordinates for ellipses encompassing 95% of the mothers in each dataset, based on height and BMI. The example that is given is for the Mysore 2 dataset.

Step 1 ***Setting up the data***

```
clear all
emysore2                                  % The file emysore2.m contains columns of data
                                          % relating to height and BMI
                                          % (complete data on both variables only),
                                          % labelled 'data1'.
[size1 size2] = size(data1)               % Calculating the size of the dataset -
                                          % size1 = column length (= 597),
                                          % size2 = row length (= 2).

for i = 1:size1                           % Storing the data as row vectors
        x1(i) = data1(i,1);               % (size [1×597]).
        y1(i) = data1(i,2);
end
```

Step 2 ***Centering axes on median height and BMI***

```
medianx1 = median(x1);                    % Calculating median values.
mediany1 = median(y1);

for i=1:size1                             % Shifting origin to median values.
        x2(i) = x1(i) - medianx1;
        y2(i) = y1(i) - mediany1;
end
```

Step 3 ***Rotating axes so parallel to line of best fit***

```
for i = 1:size1                           % Setting up design matrix.
        X(i,1) = 1.0;
        X(i,2) = x1(i);
end

y1tran= y1';                              % Transposing BMI data to become a column
                                          % vector (size [597×1]).

coeff = inv(X'*X)*X'*y1tran;              % Calculating regression coefficients.

theta = atan(coeff(2));                   % Calculating the angle required for rotation.
                                          % (using tan(θ) = opposite/adjacent =
                                          % regression slope).

for i=1:size1                             % Rotating axes so parallel to line of best
        x3(i) = cos(theta)*x2(i) + sin(theta)*y2(i);   % fit.
        y3(i) = -sin(theta)*x2(i) + cos(theta)*y2(i);
end
```

Step 4 ***Fitting an ellipse that encompasses 95% of the data***

```
ratio = (max(x3)-min(x3)) / (max(y3)-min(y3));      Calculating ratio of height range to BMI range.
checker = 0;                                        Used later to control the loop which calculate the
                                                    appropriate values for a and b to be used in the
                                                    ellipse equation - x3^2/a^2 + y 3^2/b^2 = 1.

tau = 10;                                           Used to calculate a and b (10 is an arbitrary value).

while checker < 0.5
        a = tau*ratio;                              Calculating initial values for a and b.
        b = tau;
        nooutside = round(size1*0.05);              Calculating number of datapoints required to be
                                                    outside ellipse (5% rounded = 28).
        countoutside = 0;                           Setting number of datapoints actually outside ellipse
                                                    to be zero.
        for i = 1:size1                             Determining number actually outside ellipse by
                                                    looping through each individually.
                qq(i) = (((x3(i)^2)/(a^2)) + ((y3(i)^2)/(b^2)));
                if qq(i) > 1
                        countoutside = countoutside + 1;
                end
        end
        if countoutside == nooutside                Stopping the loop once the required number of
                checker = 1;                        datapoints are outside the ellipse.
        end
        tau = tau*0.999;                            Shrinking the size of the ellipse by 0.1% before loop is
                                                    repeated.
        if countoutside > nooutside                 Terminating program if the initial ellipse is too
                stop                                small – tau must be reset.
        end
end

npts = 21                                           Setting up height values at which BMI values on
                                                    ellipse will be predicted (21 is arbitrary).
interval = 2*a / (npts-1);
for i =1:npts                                       Defining ellipse co-ordinates.
        x4(i) = -a + (i - 1)*interval;
        y4(i) = sqrt( (b^2)*( 1 - (x4(i)/a)^2 ) );
        x4(i + npts) = a - (i-1)*interval;
        y4(i + npts) = -sqrt( (b^2)*( 1 - (x4(i + 21)/a)^2 ) );
end
```

Step 5 ***Transforming co-ordinates back to original axes***

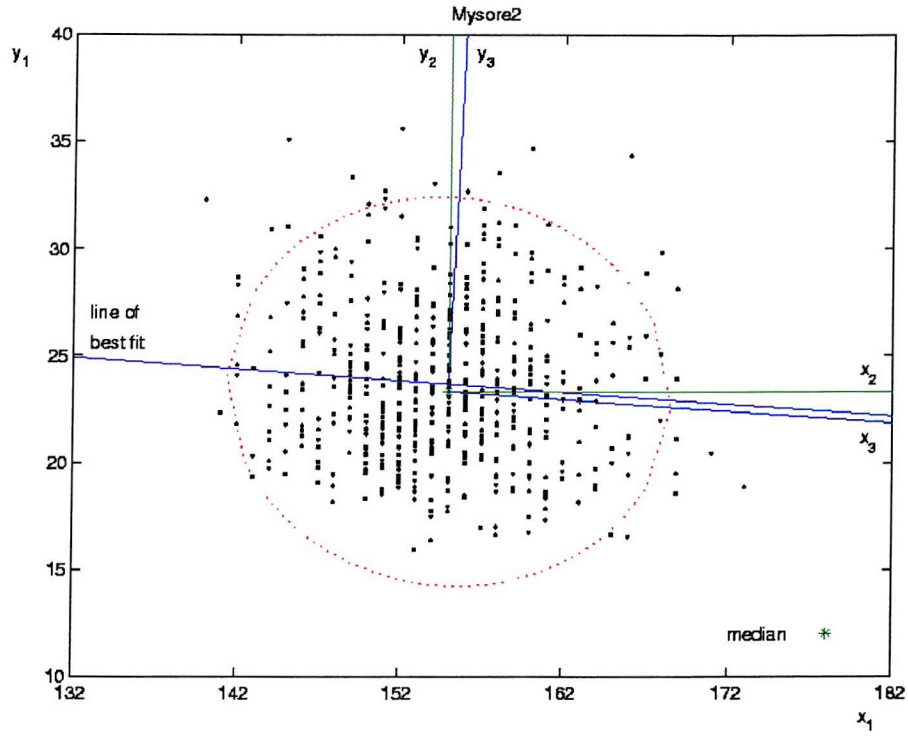
```
for i=1:2*npts                                      Rotating co-ordinates so parallel with original axes .
        x5(i) = cos(-theta)*x4(i) + sin(-theta)*y4(i);
        y5(i) = -sin(-theta)*x4(i) + cos(-theta)*y4(i);
end

for i =1:2*npts                                     Shifting origin back to (0,0).
        x6(i) = x5(i) + medianx1;
        y6(i) = y5(i) + mediany1;
end
```

Step 6 Printing ellipse co-ordinates

[x6' y6']

Printing final co-ordinates for ellipse to use in contour plots.



Appendix 4e Form of relationships between maternal height/BMI and gestation adjusted neonatal measurements (simultaneous models)

L = linear
Q = quadratic
NS = non significant

	Birthweight	Placental weight	CH length	CR length	Leg length	Head	Chest	Abdomen	MUAC	AMA	Triceps	SS	PI	Head/length	Head/abdomen	Placenta/birthweight
Southampton 1	L	L	L	L	L	L		L	L				L	NS	L	NS
Southampton 2	Q	L	L	L	L	L		L	L				L	L	NS	NS
Southampton 3	L	L	L			L		L	L			L	L	L	L	NS
Southampton 4	L	L	NS	NS	L	L		NS	L				L	L	NS	NS
Farnborough	Q	L	L			L							NS	NS		L
Isle of Man	L	Q	L			L		L					L	L	NS	NS
Aberdeen	L	L														NS
Mysore 1	L		L			NS							NS	L		
Mysore 2	L	L	L	L	NS	L		L	L	L	L	L	L	L	L	NS
Pune 1	L	L	L			L	L	NS	L	L	NS	NS	L	L	NS	NS
Kandy, Sri Lanka	L		L			L							L	L		
Beijing	L	L	L	L	L	L							L	Q		L
Kasaji, Congo	L	L	L			L	L		L	L	NS	NS	L	L		NS
Imesi, Nigeria	L	L	L			L	L						L	NS		NS
Kingston 1	L	L	L	L	NS	L	Q	L	L				NS	NS	NS	NS
Kingston 2	L	NS	L	NS	NS	NS							NS	NS		NS

Appendix 5 Father to baby relationships

Appendix 5a Median paternal measurements

		Height (cm)	BMI (kg/m^2)
Southampton 1	Median	**178.0**	
	IQR	173.0,183.0	
	N	543	
Southampton 2	Median	**176.0**	
	IQR	171.0,181.0	
	N	511	
Southampton 4	Median	**177.8**	
	IQR	174.8,182.9	
	N	98	
Isle of Man	Median	**175.3**	
	IQR	171.5,182.9	
	N	385	
Mysore 1	Median	**165.9**	**23.6**
	IQR	161.9,170.5	20.8,26.4
	N	690	690
Mysore 2	Median	**167.3**	**23.1**
	IQR	163.0,171.1	20.3,25.5
	N	496	496
Pune 1	Median	**164.7**	**19.0**
	IQR	160.7,168.6	17.6,20.8
	N	599	599
Kasaji, Congo	Median	**164.0**	**19.5**
	IQR	159.8,169.3	18.3,20.7
	N	217	215
Imesi, Nigeria	Median	**170.2**	**21.4**
	IQR	165.1,172.7	20.4,22.9
	N	194	194

Appendix 5b Relationships between paternal and neonatal anthropometry

p≥0.1 p<0.1 p<0.05 p<0.01

Paternal predictors	Height (cm)		BMI (kg/m^2)	
	Linear	Quadratic	Linear	Quadratic
Birthweight (g)				
Southampton 1	526.04			
Southampton 2	625.58			
Southampton 4	536.52			
Isle of Man	693.14			
Mysore 1	1070.52	-5833.35	153.17	
Mysore 2	663.69		189.91	-321.21
Pune 1	450.69		167.73	
Kasaji, Congo	1216.39		558.16	
Imesi, Nigeria	-58.65		-24.94	
Placental weight (g)				
Southampton 1	146.43			
Southampton 2	-37.50			
Southampton 4	-55.50			
Isle of Man	131.58			
Mysore 1	33.95		11.90	
Mysore 2	85.44		28.34	
Pune 1	48.32		37.84	
Kasaji, Congo	112.96		69.90	
Imesi, Nigeria	1.28		19.08	
CH length (cm)				
Southampton 1	0.04			
Southampton 2	0.05			
Southampton 4	0.07			
Isle of Man	0.04			
Mysore 1	0.03		0.01	
Mysore 2	0.05		0.04	-0.01
Pune 1	0.05		0.05	
Kasaji, Congo	0.05		0.23	
Imesi, Nigeria	0.03		-0.08	
CR length (cm)				
Southampton 1	0.02			
Southampton 2	0.03			
Southampton 4	0.03			
Isle of Man				
Mysore 1				
Mysore 2	0.02		0.06	-0.01
Pune 1				
Kasaji, Congo				
Imesi, Nigeria				
Leg length (cm)				
Southampton 1	0.02			
Southampton 2	0.02			
Southampton 4	0.04			
Isle of Man				
Mysore 1				
Mysore 2	0.03		-0.02	
Pune 1				
Kasaji, Congo				
Imesi, Nigeria				

Paternal predictors	Height (cm)		BMI (kg/m^2)	
	Linear	Quadratic	Linear	Quadratic
Head (cm)				
Southampton 1	0.02			
Southampton 2	0.01			
Southampton 4	0.01			
Isle of Man	0.01			
Mysore 1	0.02		0.002	
Mysore 2	0.01		0.06	-0.01
Pune 1	0.02		0.03	
Kasaji, Congo	0.02		0.11	
Imesi, Nigeria	0.003		0.07	
Chest (cm)				
Southampton 1				
Southampton 2				
Southampton 4				
Isle of Man				
Mysore 1				
Mysore 2				
Pune 1	0.02		0.07	
Kasaji, Congo	0.05		0.22	
Imesi, Nigeria	0.01		-0.03	
Abdomen (cm)				
Southampton 1	0.02			
Southampton 2	0.01			
Southampton 4	0.03			
Isle of Man	0.02			
Mysore 1				
Mysore 2	0.01		0.07	-0.01
Pune 1	0.02		0.06	
Kasaji, Congo				
Imesi, Nigeria				
MUAC (cm)				
Southampton 1	0.001			
Southampton 2	0.01			
Southampton 4	0.003			
Isle of Man				
Mysore 1				
Mysore 2	0.01		0.04	
Pune 1	0.02		0.04	
Kasaji, Congo	0.02		0.08	
Imesi, Nigeria				
AMA (cm^2)				
Southampton 1				
Southampton 2				
Southampton 4				
Isle of Man				
Mysore 1				
Mysore 2	0.02		0.08	
Pune 1	0.05		0.07	
Kasaji, Congo	0.04		0.16	
Imesi, Nigeria				

Paternal predictors	Height (cm)		BMI (kg/m^2)	
	Linear	Quadratic	Linear	Quadratic
Triceps (mm)				
Southampton 1				
Southampton 2				
Southampton 4				
Isle of Man				
Mysore 1				
Mysore 2	0.003		0.04	
Pune 1	-0.003		0.03	
Kasaji, Congo	0.02		0.04	
Imesi, Nigeria				
Subscapular (mm)				
Southampton 1				
Southampton 2				
Southampton 4				
Isle of Man				
Mysore 1				
Mysore 2	0.003		0.03	
Pune 1	-0.002		0.02	
Kasaji, Congo	0.01		0.06	
Imesi, Nigeria				
PI (kg/m^3)				
Southampton 1	-0.03			
Southampton 2	-0.03			
Southampton 4	-0.08			
Isle of Man	-0.01			
Mysore 1	0.05		0.11	
Mysore 2	-0.02		0.12	
Pune 1	-0.04		0.07	
Kasaji, Congo	0.03		0.14	
Imesi, Nigeria	-0.02		0.20	
Head/length (%)				
Southampton 1	-3.11			
Southampton 2	-5.60			
Southampton 4	-8.86			
Isle of Man	-2.83	28.45		
Mysore 1	-0.48		-0.13	
Mysore 2	-4.66	-45.64	0.75	
Pune 1	-3.05	-37.08	-0.16	
Kasaji, Congo	0.19		-0.61	
Imesi, Nigeria	-3.27		2.75	
Head/abdomen (%)				
Southampton 1	-0.09			
Southampton 2	-1.50			
Southampton 4	-7.76			
Isle of Man	-2.18			
Mysore 1				
Mysore 2	-0.48		-0.95	
Pune 1	0.68		-1.44	
Kasaji, Congo				
Imesi, Nigeria				

Paternal predictors	Height (cm)		BMI (kg/m^2)	
	Linear	Quadratic	Linear	Quadratic
Placenta/birthweight (%)				
Southampton 1	1.44			
Southampton 2	-4.15			
Southampton 4	-3.83			
Isle of Man	1.01			
Mysore 1	-3.39		-0.19	
Mysore 2	0.02		0.03	
Pune 1	-0.84		0.55	
Kasaji, Congo	-1.24		-0.19	
Imesi, Nigeria	1.01		-1.06	

Appendix 6 Relationships with blood pressure in later life

Appendix 6a US blood pressure standards

Age (years)	Males – mean(SD) mm Hg	Females – mean (SD) mm Hg
1	90.8(9.0)	91.3(9.7)
2	94.3(10.0)	94.3(10.2)
3	9038(13.2)	90.3(13.1)
4	91.1(11.9)	90.7(13.0)
5	94.4(10.9)	64.2(10.6)
6	96.2(10.1)	65.4(10.5)
7	97.8(10.4)	96.5(10.3)
8	98.7(10.0)	98.3(10.3)
9	100.8(10.1)	100.2(10.8)
10	102.6(10.1)	102.2(10.2)
11	104.0(9.9)	104.4(10.2)
12	106.4(10.1)	107.0(10.2)
13	108.4(11.6)	107.4(11.2)
14	110.7(12.2)	108.0(11.1)
15	112.9(12.4)	107.6(11.3)
16	114.7(12.3)	109.1(11.1)
17	117.7(12.2)	110.2(11.1)
18-24	123.5(13.0)	114.8(13.1)
25-34	125.5(13.9)	116.7(14.1)
35-44	127.7(15.4)	123.6(19.2)
45-54	135.3(20.7)	132.9(24.4)
55-64	139.7(20.8)	144.0(25.6)
65-74	146.9(24.7)	152.5(25.2)

Appendix 6b Height, BMI and room temperature effects on SBP SD score
(Subject's own height and BMI and room temperature at time of SBP measurement)
$p \geq 0.1$ $p<0.1$ $p<0.05$ $p<0.01$

	Height (10cm)		BMI (kg/m2×10)		Room temperature (°)	
	Linear	Quadratic	Linear	Quadratic	Linear	Quadratic
Preston	0.19		0.44		-0.001	
Sheffield	0.08		0.17		0.02	
Farnborough	0.20		0.70		-0.05	
Aberdeen	0.15	0.17	0.29	-0.31	0.04	
Mysore 1a	0.05		0.49	-1.68	-0.03	
Mysore 1b	-0.10		0.40		-0.08	
Beijing	0.08		0.80		-0.02	
Kingston 1	0.43		1.27			
Kingston 2	0.33		1.24			
WHO Sweden	0.15		0.56		-0.01	
WHO Chile	0.02		1.02		-0.01	
WHO Guatemala	0.03		0.71		0.01	
WHO China	0.16		0.20		-0.02	
WHO Nigeria	0.11		1.22		-0.01	

Appendix 6c Mean SBP SD scores

		SBP
Preston	Mean	**0.71**
	SD	0.95
	N	347
Sheffield	Mean	**-0.12**
	SD	0.93
	N	281
Farnborough	Mean	**-0.09**
	SD	0.71
	N	335
Aberdeen	Mean	**0.66**
	SD	0.83
	N	233
Mysore 1a	Mean	**-0.21**
	SD	0.83
	N	660
Mysore 1b	Mean	**-0.10**
	SD	**0.81**
	N	400
Beijing	Mean	**-0.28**
	SD	0.72
	N	562
Kingston 1	Mean	**0.05**
	SD	0.51
	N	323
Kingston 2	Mean	**-0.91**
	SD	0.76
	N	70
WHO Sweden	Mean	**0.92**
	SD	0.58
	N	323
WHO Chile	Mean	**1.37**
	SD	0.86
	N	323
WHO Guatemala	Mean	**0.27**
	SD	0.50
	N	323
WHO China	Mean	**0.75**
	SD	0.64
	N	323
WHO Nigeria	Mean	**0.80**
	SD	0.73
	N	323

Appendix 6d Relationships between neonatal/maternal anthropometry and SBP SD score

p≥0.1 p<0.1 p<0.05 p<0.01

	Birthweight (kg)	Placenta (kg)	CH length (10cm)	Head (10cm)
Preston	-0.35	0.11	-0.32	-0.38
Sheffield	-0.11	-0.34	0.07	-0.16
Farnborough	-0.20	-0.34	-0.25	-0.79
Aberdeen	-0.31	-0.09		
Mysore 1a	-0.03	-0.66	-0.14	-0.10
Mysore 1b	0.02		-0.04	0.08
Beijing	-0.20	-0.71	-0.27	-0.29
Kingston 1	-0.17	-0.32	-0.13	-0.15
Kingston 2	0.15	-0.42	0.22	0.13
WHO Sweden	-0.02		0.31	-0.15
WHO Chile	-0.29		-0.49	-0.70
WHO Guatemala	-0.22 (quadratic=0.45)		-0.37	-1.00
WHO China	0.02		-0.11	-0.43
WHO Nigeria	0.03		0.31	0.10

	PI (kg/m^3*10)	Head/length (ratio)	Placenta/birthweight (ratio)
Preston	-0.32	0.19	4.1
Sheffield	-0.18	-0.58	-2.0
Farnborough	0.02	-0.26	0.75
Aberdeen			2.02
Mysore 1a	0.06	0.52	-1.27
Mysore 1b	0.03	0.58	
Beijing	-0.27	0.26	-0.24
Kingston 1	-0.11	0.56	0.42
Kingston 2	-0.12	-0.92	-3.5
WHO Sweden	-0.26	-2.18	
WHO Chile	-0.20	-0.27	
WHO Guatemala	-0.13	-0.002	
WHO China	0.07	-0.93	
WHO Nigeria	-0.20	-1.57	

	Maternal height (10cm)	Maternal BMI (kg/m^2*10)
Preston		
Sheffield		
Farnborough	-0.08	0.05
Aberdeen	-0.06	-0.11
Mysore 1a	-0.03	
Mysore 1b	-0.05 (quadratic=0.27)	
Beijing	-0.14	0.25
Kingston 1	-0.05	-0.10
Kingston 2	0.10	-0.02
WHO Sweden	0.06	
WHO Chile	-0.08	
WHO Guatemala	0.02	
WHO China	0.04	
WHO Nigeria	0.02	

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